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PRINCIPLES OF SURGICAL PRACTICE

THE BACTERIOLOGICAL AND SURGICAL PRINCIPLES IN THE MANAGEMENT OF SURGICAL SEPTICEMIA

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IN A case of septicemia due to pyogenic or necrotizing organisms it is the surgeon's responsibility to locate the distributing focus and, if it is possible, to remove, drain, or isolate it.

Definition. The present generally accepted meaning of the word septicemia is an illness characterized by an intermittent or sustained fever with malaise and prostration accompanied by the continued presence of bacteria in the blood stream, which can be repeatedly cultivated from the blood on artificial media.

Pathogenesis. When bacteria enter the physiological interior of the body, the actual number is probably small—tens, scores, perhaps hundreds, but not thousands or millions. They are usually introduced through a break in the surface either of the skin or the mucous membrane, which serves as the primary defense of the body. They are then surrounded by dead or injured tissue, or foreign bodies. Many of them are not in a favorable growth phase to adapt themselves to the new environment and they fail to grow and metabolize and are destroyed by the phagocytes which are attracted to the site of the injury. A few of them, however, find the environment suitable for their metabolic activities, and they may be protected from the local defenses by the injured tissue or by the foreign bodies. They proceed to multiply and form a colony and produce their poisons. These poisons may attract or repel the phagocytic wandering cells or they may liquefy the dead tissue or kill or injure living tissue. If leucocytes are attracted, the organisms may be phagocyted by them. Sometimes they are killed by the phagocytes and sometimes they continue to grow within the phagocytes until the bacterial colony breaks the cell membrane and destroys the cell. Sometimes they are carried into the lymph system or the blood vessels by the phagocytic cell. If they gain entrance into the former they may be filtered out by the lymph glands and either be destroyed in the glands or continue to grow and break down the gland tissue and thus form a metastatic focus. If they gain entrance with a phagocyte into the blood stream they may be destroyed there or be carried to other parts of the body, be caught and destroyed by the endothelial phagocytes, or start a new focus in some capillary channel in some favorable location.

If they are not carried by phagocytes but continue to grow at the site of entrance they sooner or later come into contact with lymph or blood capillaries. The colony is surrounded by a concentrated zone of bacterial poison which acts upon the surrounding tissue, but is diluted and to some extent carried away by the circulating fluids and thus gives rise to general symptoms of intoxication. Individual organisms in the periphery of the colony are also subject to the movement of the circulatory lymph and may be carried away by it. This fluid makes its way into the lymph system, but the organisms are temporarily checked by the closed system of the endothelial membranes. It may be that individual organisms are carried in between the endothelial cells with the fluid, or the organisms may multiply and start a new colony on the outer surface of the capillary wall. Sooner or later, the poison produced by the main colony or the secondary colony

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of bacteria acts upon the capillary wall. It may either liquefy it or produce an inflammatory reaction resulting in closure of the capillary wall or clotting of the fluid within it. The same effect is produced on larger vessels, venules and arterioles. As the process advances the larger veins and arteries become thrombosed and then liquefied, a sterile portion of clot progressing in both directions ahead of the infection and liquefaction. All of these steps can be seen in microscopic slides of inflammatory processes in tissue.

Pathology. The portal of entry, particularly in children, may be hardly noticeable and the major focus of infection may be deep within the body. In the majority of cases, however, the major focus is at or near the place where the organism entered the body. In the gross, the primary focus generally presents either a diffuse cellulitis or an abscess containing pus, which is a more or less homogeneous fluid made up of dead and living leucocytes, dead and living bacteria, and cellular débris. A Gram-stained slide of the abscess wall shows countless organisms in the exudate on the surface, but the number diminishes rapidly from the surface inward toward normal tissue. When an abscess is opened with the knife there is bleeding from the portion of the wall which is cut but not from the wall of the abscess itself. In that wall there are innumerable blood vessels which have become thrombosed and then liquefied and the end of every one is plugged with an infected thrombus. Out in the periphery, the clots filling these vessels may be sterile, but as the process advances in untreated cases the organisms in the wall of the abscess advance steadily within the blood vessels with a successive infection and liquefaction of these myriads of clots. When the clot reaches a large vessel it may break off and be carried peripherally if that vessel is an artery, or centrally if it is a vein, and be filtered out by some capillary too small to let it pass. If the clot is small and sterile nothing of importance happens. If it is large enough it may mechanically cause local gangrene or even death, as for example, a large pulmonary embolus. If the clot contains bacteria, it may produce another focus of infection from which the process may be repeated.

It is not surprising, therefore, that from any infected focus, either primary or secondary, there is a constant entrance of bacteria into the blood stream either as individual organisms or incorporated in a blood clot. The number will depend to a considerable extent upon the virulence of the organisms, their ability to multiply within the area of infection, and the potency of their toxins to kill or injure tissue.

Because of the prevalence of serious infections in war wounds, the opportunity was afforded the army pathologists to study a large number of fatal cases which had yielded positive blood cultures before death or at autopsy. Pappenheimer (18) and others found that almost invariably in these cases there could be found a gross focus of infection in some organ or body cavity in the walls of which a suppurative thrombophlebitis existed which opened directly into the blood stream. In Neuhof's series (17) of 150 cases of surgical septicemia in civilian practice a suppurative thrombophlebitis was found in 41 per cent.

In the majority of instances in fatal cases, there are multiple metastatic foci of suppuration where infected emboli or individual organisms have lodged and have formed bacterial colonies and are repeating to some extent the destruction of tissue which occurred at the primary site. A certain number of cases also develop a vegetative endocarditis, a potent source of infected emboli on the arterial side. In cases which terminate in recovery we may assume that the process is held in check by a fixation of the clots within the blood vessels and a subsidence of the infection within the clots either with or without the help of the therapeutic procedures described below.

Experimental conceptions. In experimental work it has been known for a long time that living bacteria could be introduced directly into the blood stream of animals and that death depended upon the kind, the virulence, and the number of organisms injected. It was found that many organisms were entirely without effect even when injected by the billions, and that in the case of many organisms of high virulence there is generally a fixed minimal lethal dose of several thousand organisms. For example, by frequent animal passage of hemolytic streptococci, Dochez and his co-workers (6) were able to increase the virulence of only 20 per cent of his strains to the point where 1,000 organisms would kill a mouse. This has been repeatedly confirmed so that we can be sure that the animal body and probably the human body have the power to destroy many highly virulent organisms when they are introduced into the blood stream.

Hopkins and Parker (9), among others, some years ago tried to discover the mechanism of this phenomenon. After determining the minimal lethal dose of a strain of hemolytic streptococcus for rabbits, they injected both lethal and sublethal doses into the blood stream of a series of these animals, and similar or larger doses into the blood stream of resistant cats. They immediately estimated the number of organisms per

cubic centimeter of blood and made repeated counts at frequent intervals. They found that the number of organisms in the circulating blood rapidly diminished.

In the sublethal doses the organisms usually disappeared completely in from one to two hours and did not reappear. In the lethal doses they rapidly diminished in number and in many instances completely disappeared, but after a brief interval they began to reappear in ever-increasing numbers until the death of the animal four or five days later. Furthermore, repeated doses of organisms were similarly rapidly "cleared" from the blood stream. When the resistant cats were killed and examined one-half hour after the injection, the bacteria could be found in large numbers in the endothelial phagocytes of the lungs. Cultures from the ground-up tissue of various organs yielded enormous numbers of bacteria from the lungs, many from the liver and spleen, a few from the bone marrow and lymph glands, and few or none from the blood, muscles, or kidneys. Cultures from cats killed several hours after the injection showed a marked decrease of bacteria in the lungs and liver, but not such a great decrease in the other tissues. If pieces of lung and liver tissue were excised the decrease in the number of organisms still took place, but the number increased in the excised spleen. Extracts of lung did not have the same bactericidal action. These workers concluded that the chief agents in clearing the blood of organisms were the endothelial cells of the lungs and liver. In lethal doses bacteria distributed from other foci overwhelmed this clearing mechanism.

Experimental septicemia is different from clinical septicemia in at least one important respect. In the former, enormous doses of bacteria are introduced at one time into the circulation, while in the latter, small numbers are introduced into the blood stream more or less continuously. The mechanism by which these bacteria are destroyed, however, is essentially the same.

The body defenses. The clearing mechanism of the blood is both cellular and humoral. It has been studied by numerous workers in the field of immunology. Kolmer (11) has recently summed it up as follows:

The cellular elements carry on phagocytosis of bacteria and comprise the polymorphonuclear leucocytes, the macrophages of the lungs, and the histiocytes of the reticulo-endothelial system. The humoral components include the various immune elements in the blood, natural or acquired, agglutinins, opsonins, bacteriolysins, antitoxins, leucines, plakins, and complement.

Under the most favorable conditions of artificial cultivation, bacteria multiply about once every half hour. Their multiplication within the blood stream must be very much slower than this because it has been shown repeatedly that whole blood is not a favorable medium for bacterial growth. The blood makes one complete circuit of the body every minute, passing through the endothelial lined capillaries of the periphery, the lungs, and possibly the liver also with each round. An organism has to run the gauntlet of phagocytic cells 60 or more times before it has time to multiply. It is extremely unlikely that there is any multiplication of bacteria in the blood stream until the blood has ceased to flow.

When a blood culture is taken from a peripheral vein at the elbow any organism which is recovered has passed the gauntlet of the lung capillaries and the capillaries of the periphery of the forearm or hand. The lungs filter out most of the embolic clots, and the endothelial cells pick up the individual organisms. If an attempt is made to determine the number of organisms per cubic centimeter of the peripheral blood by means of agar pour plates, we find that even extremely sick patients seldom yield more than 100 colonies per cubic centimeter of blood. This is a surprisingly small number if one considers that an ordinary twenty-four-hour broth culture of bacteria has anywhere from 1 to 5 billion organisms per cubic centimeter.

The presence of bacteria in the blood stream is simply an indication of what is going on around the distributing focus. The continued presence of bacteria in the blood indicates that the focus is distributing organisms faster than the clearing mechanism can take care of them.

Bacteriology. For the rational treatment of sepsis it is, of course, of vital importance to know as soon as possible which organism is causing the disease. This knowledge may at once indicate whether the patient should be treated by medical or surgical methods. Certain of the organisms commonly found in the blood render the case medical because there is a tendency toward self-limitation and resolution without extensive destruction of tissue. For example, the meningococcus, the gonococcus, the bacillus influenzæ, and, for the most part, the pneumococcus fall into this category. Others have a tendency to cause necrosis of tissue and the localization of pus. They are called pyogenic or necrotizing organisms. When these are found, in the present state of our medical knowledge, the case is rendered surgical, for the situation as far as the patient is concerned may

be greatly benefited by the surgical procedures of excision, incision, or isolation. The organisms responsible for surgical sepsis in the order of their frequency in Neuhof's series (17) are as follows:

1. Hemolytic streptococcus
2. Hemolytic staphylococcus aureus
3. Non-hemolytic staphylococcus aureus
4. Non-hemolytic streptococcus
5. Bacillus coli
6. Anaerobic non-hemolytic streptococcus
7. Staphylococcus albus
8. Bacillus mucosus capsulatus

Scott's series (20) and our own roughly correspond to Neuhof's.

An early knowledge of the causative organism may point to a hidden focus, for we know that certain organisms have a predilection for certain tissues, and in cases of sepsis are generally found in certain places in the body. Conversely, if the lesion is clinically apparent, experience leads one to predict with some degree of certainty which organism will be found in the blood, and its clinical behavior can be foreseen to some extent; for example: the hemolytic streptococcus is by far the most common organism in sepsis of otitic origin, infection of tendon sheaths, or in sepsis from a diffuse cellulitis, while the staphylococcus aureus is more commonly associated with sepsis following carbuncles, suppurative parotitis, well-localized abscesses generally, and osteomyelitis. Bacillus coli is the common organism in sepsis from peritonitis and from bladder and kidney-pelvis infections. The non-hemolytic streptococcus is most often associated with the grave face and neck infections of dental origin. On the other hand, the hemolytic streptococcus and the staphylococcus aureus share equally in the incidence of sepsis following severe infections of the kidney parenchyma. The bacillus coli and the non-hemolytic streptococcus are equally involved and often found together in the liver and peritoneal abscesses, and either or both together are occasionally found in the blood in the later stages of these diseases. The hemolytic streptococcus and the hemolytic staphylococcus aureus share equally in the incidence of vegetative endocarditis.

Clinical Manifestations. Scott (20) groups the surgical septicemia cases into four groups:

1. The rapidly progressive case, which is fulminating and usually fatal.
2. The plateau type of case, which slowly terminates in recovery or slowly loses ground.
3. The transient cases, which terminate in recovery quickly and often spontaneously.
4. The terminal cases, which develop during the course of some debilitating disease.

Neuhof (17) has grouped his cases more or less anatomically, according to the type of the primary focus, e.g., bone and joint, mastoid, subcutaneous abscess, carbuncle and cellulitis, liver and gall bladder, and postpartum. He found that in his series of 150 cases chills occurred in less than half of the total number, but in more than half of the cases with phlebitis. Fever was spiking in only one-third of his cases and sustained in almost as many. Metastatic foci developed in 43 per cent of his cases and multiple lung abscesses in 28 per cent.

THE SURGICAL PRINCIPLES OF TREATING SEPTICEMIA

Prophylaxis. In considering the surgical treatment of septicemia, prophylaxis must be given first consideration because it is so much more effective than active treatment. It is true that many cases of infection come to the surgeon with the blood stream already invaded, but a far greater number of patients come to him with a seemingly trivial condition, and a septicemia develops because of the improper handling of the primary situation. These cases fall largely into two groups.

The first group comprises the punctured or lacerated wounds and those wounds caused by automobile accidents. The proper care of punctured wounds is most difficult in the individual case. These wounds occur frequently in doctors and nurses and are due to pin pricks or needle punctures received during the care of an infected case. Often the depth is not known. The question arises whether they should be opened widely at once or let alone until general symptoms develop. Except in rare instances in which the inoculation of virulent organisms is known to be heavy, soaking of the whole part in hot water at from 108 to 112 degrees F., alternately in and out, for an hour at a time will abort the great majority of infections. With the first sign of inflammation, however, the wound should be opened to its depth, the soaking continued, and an ice bag applied almost continuously to the regional lymph glands.

With regard to lacerated wounds, many doctors pay too little heed to the necessity for thorough cleansing of the wound and the mechanical removal of all foreign bodies with soap and water and a sterile brush. If the edges are contused they must be débrided under block or general anesthesia until normal tissues are everywhere visible. Then if the wound is recent (within two hours) primary suture may be considered, but the sutures must be applied so that any exudate

may easily escape. If the wound is more than two hours old, primary suture should be done only in highly vascularized tissues, like the face or scalp. The wound should then be closed loosely with a small rubber drain to let out the exudate, and a free opening should be made if any inflammation subsequently appears. Too many lacerated wounds are inadequately cleansed, too poorly débrided, and too firmly closed.

The second group comprises those relatively minor and well-localized infections which are traumatized, and become rapidly spreading vicious affairs. The lowly pimple which is pricked or squeezed, usually by the patient; the boil or carbuncle which is pricked or squeezed, or carbolized or inadequately incised with an expression of pus, by the doctor all too frequently; infected teeth or tonsils which are removed during the stages of acute inflammation, all fall into this category. If boils or carbuncles are to be incised or excised, it should be done adequately with the incision extending beyond the area of induration, and with the minimum of trauma. Teeth and tonsils should be removed only after the acute process has subsided and packing should never be left in for more than an hour. On the other hand, in acute otitis media the ear drums may require early opening to minimize the possibility of mastoid involvement.

Active Treatment. In the presence of a septicemia caused by the pyogenic or necrotizing organisms, it is the surgeon's responsibility to find and, if possible, eradicate the distributing focus, with the possibility ever in mind that there may be a suppurative phlebitis in the neighborhood of the focus requiring proximal ligation or excision.

In the great majority of cases there is an abscess cavity containing pus, surrounded by a zone of cellulitis. If the process can be excised completely without sacrifice of important function or form, the whole process should be excised. If not, an ample incision should be made to the limits and slightly beyond the limits of the involved tissue. I have never seen any harm done from a clean-cut incision into normal tissues beyond the limits of an infection, but I have seen harm done, as evidenced by rapid spread of the infection, by an inadequate incision, which is so often accompanied by a breaking down of the inner wall by finger manipulation within the cavity.

If there is any suspicion of involvement of the neighboring vein, it should be proximally ligated in a normal area, and then the involved portion should be opened and drained, or excised if that is possible. Any involved radicals likewise should be followed up until normal vein lumen is reached. Neuhof (16) calls attention to the relatively low mortality in septicemia of otitic origin with lateral-sinus thrombosis, in which it is common practice to tie off the jugular vein and its facial radicals. He exhorts the general surgeon to carry out a similar procedure when such veins as the basilic, cephalic, brachial, axillary, femoral, saphenous, or iliac are similarly involved.

If there are no surface indications to point out the distributing focus, a search must be made for it within the body. It may be revealed by the symptoms or physical signs. Pain is usually present, although it is often absent in chest infections in which shortness of breath may indicate a lung abscess or empyema. If an abscess is connected with a bronchus there is, of course, more or less purulent sputum. A liver or subphrenic abscess may be surprisingly free from pain, but the physical signs of dullness at the lung base, tenderness on compression of the ribs, or the x-ray evidence of fixation of the diaphragm may make the diagnosis clear.

In kidney infections pain may be minimal, but tenderness and swelling are frequently present, and the presence of pus in the urine if the ureter is patent indicates disease there, particularly when cystoscopy reveals that the bladder is normal and pus is coming from one ureter.

Intraperitoneal abscesses can frequently be revealed by careful abdominal examination when indurated, tender masses may be felt unless they are subphrenic or pelvic. A rectal examination may reveal a pelvic abscess or a large, tender prostate which is not infrequently the primary focus of a septicemia.

The spleen is occasionally the site of a single abscess. The enlargement and local tenderness will usually suggest the presence of such a lesion.

Perhaps the most difficult of all of the internal distributing foci to discover is endocarditis, which is usually not primary except for the streptococcus-viridans group. The hemolytic streptococcus and the staphylococcus aureus may produce vegetations on the heart valves late in the course of septicemia, and their presence is often not revealed until gradually increasing cardiac murmurs have developed.

As far as I know there are no instances of recovery in cases of septicemia which have developed vegetative endocarditis with either of these two organisms. The presence of the lesion is too uncertain to warrant an exploratory operation for the removal of these vegetations, although the attempt will be made some day. The other internal

foci mentioned have been and should be surgically approached. Single abscesses in the liver, kidney, or lung may be adequately drained, but multiple abscesses in these organs, be they diffusely scattered or conglomerate, are only rarely successfully approached surgically, although the attempt should always be made.

If only one kidney is involved by multiple abscesses, a nephrectomy is essential. It is often difficult or impossible to tell whether or not the other kidney is involved in a similar process, and the urological surgeon is frequently loath to remove the obviously sick kidney, but the chance of recovery if it is left in is so remote that it should be removed even with this uncertainty.

Single abscess or multiple abscesses of the spleen may be controlled by splenectomy if the infection has not already spread through the portal vein to the liver.

It may be very difficult to locate osteomyelitis or differentiate it from suppurative arthritis, particularly in the region of the hip joint. Usually the severe pain, the local tenderness, and later the swelling over the bone reveal the focus there. Suppurative foci in joints are more easily found by a routine examination of all of the joints. Unless the capsule has been broken, the intense pain on movement is almost a pathognomonic sign.

After the primary focus has been found and properly excised or incised and drained, the patient should be examined completely daily for evidence of metastatic lesions. These may be revealed in a co-operative patient by swelling pain and tenderness, but if the patient's sensorium has been dulled by his illness or by sedatives, these areas can often be found only by careful palpation to determine induration, swelling, or fluctuation. Redness may or may not be present. Occasionally the patient tries to hide the metastatic focus in order to avoid another operation, but all such approachable lesions must be widely opened and adequately drained to prevent, if possible, such foci from becoming in their turn distributing foci with suppurative phlebitis in the neighboring vein and all of the dangers attached thereto.

The criterion of adequacy in the surgical treatment of either the primary or secondary foci in septicemia is the subsequent presence or absence of the organisms in the blood. If the distribution can be arrested, the organisms will rapidly disappear from the blood. If they continue, the surgeon is faced with the necessity of finding another focus or of tying off or excising an involved vein. He must never rest, however, until a succession of negative blood cultures assures him that the infection is at last under control.

Chemotherapy in surgical septicemia. Ever since Ehrlich's and Hata's classical work on salvarsan and syphilis, numerous research workers have striven to find some chemical agent equally effective for bacteria. During the last twenty years attention has been focused on various dyes and these have been used both locally and intravenously with occasional apparent success. They have recently fallen into disrepute as evidence seemed to accumulate that they usually did more harm than good; acriflavine, gentian violet, and lately mercurochrome came and went, and lately metaphen in a careful study has proved to be disappointing (8). In 1935, however, Domagk (7) observed that a red dye called prontosil had a striking effect on hemolytic streptococcus sepsis in mice and rabbits. His results were soon confirmed by Levaditi and Vaisman (12), and shortly thereafter the clinical success of this agent, as well as that of a simpler form of the substance, sulfanilamide, in the treatment of hemolytic streptococcus puerperal fever was demonstrated by Colebrook (4). Its application to other types of infection with this and other organisms was tried at once and its limitations and scope have not yet been determined, but it is evident that we have for the first time a medication which will greatly facilitate the treatment of hemolytic streptococcus septicemia, and recent reports indicate the possibility that similar substances will be found equally potent against related organisms. Certainly renewed interest in chemotherapy has been aroused by this truly epoch-making discovery. The simpler form, sulfanilamide, is now in general use. It is relatively non-toxic and is readily absorbed from the alimentary tract when taken by mouth. The dose of 1 gm. for every 20 lb. of body weight is usually sufficient to maintain a concentration of about 10 mgm. per 100 c.cm. of blood, but this should be determined frequently and the dose varied in order to maintain this level to control the spread of the infection through the blood stream. This medication, however, does not obviate the necessity for the adequate surgical approach to a distributing focus, either primary or secondary, in cases of hemolytic streptococcus septicemia. In very severe cases this dose may be increased by 50 or 100 per cent and should be maintained for three or four days after the clinical subsidence of the symptoms, and then reduced to half the normal dose for a week or ten days. In a certain number of individuals having an idiosyncrasy for this drug, toxic symptoms as evidenced by a fall of red or white cells, jaundice, high fever, or delirium may necessitate abandonment of the drug in any given case.

Bacteriophage therapy in septicemia. Just as in chemotherapy there are limitations to the use of certain substances, there are very limited spheres in which bacteriophage therapy can be counted on to obtain significant results. Benefit depends also upon the most careful preparation and administration of this biological substance. Fortunately, the best field for the operation of bacteriophage is just where chemotherapy is impotent, namely, in staphylococcus aureus and in bacillus-coli infections. Favorable reports have been submitted by MacNeal (15), by Raiga (19), and others; also Longacre, Jern, and the writer have a report in the process of preparation, in which a series of cases of staphylococcus septicemia treated with bacteriophage yielded an unexpectedly high recovery. We are of the belief that other workers do not fully appreciate the importance of using potent phages. Jern and the writer (10) have pointed out a method of preparing potent phages which not only clears the culture of the causative organisms, but renders it incapable of growth when the cleared suspension is plated on blood agar. When we subject the phage to this rigid test for potency, we find that we obtain a higher percentage of cures than if we set simple clearing of the culture as the criterion of potency. Our procedure is to start with a phage potent for the organism in question diluted ten times in saline. The dose is started at 1 c.cm. of this one to ten dilution and the subsequent doses at hourly intervals are 2, 5, 10, 20, 30, and 40 c.cm. If a reaction is obtained with any of these doses the treatment is stopped for the day and that reacting dose is repeated next day. If there is no reaction from the 108 c.cm. in divided doses, a single dose of 100 c.cm. is given next day and is repeated in twelve hours. If tolerated, this dose may be gradually raised to 500 c.cm. twice a day and continued until there has been a fall in temperature and a subsidence of symptoms. Again it cannot be too strongly stressed that bacteriophage therapy does not obviate the necessity for an adequate surgical approach to the primary or secondary distributing foci, which after incision should be bathed daily or twice daily with the bacteriophage.

Fixation abscess in surgical septicemia. One finds in the literature from time to time the persistent use of a "fixation" abscess advocated many years ago by both French and German authors. The injection of sterile irritants such as turpentine under the skin, which produces an abscess, generally causes an increased leucocytosis in the peripheral blood which may be over and above that called forth by the septicemia itself. However, in such cases it has not been clearly shown that this increases in any way the resistance of the patient or modifies the course of the infection, although clinical reports, such as that of Cellan-Jones (3), lead others to adopt it as a therapeutic procedure.

Animal charcoal intravenous injections. Some striking clinical results have been reported by a number of authors following the intravenous injection of aqueous suspensions of animal charcoal in cases of septicemia. St. Jaques (21) has recently reported a small series of cases so treated, but does not give clear-cut evidence of its efficacy. He quotes Frazer who, he states, found by experimentation that charcoal absorbs toxin, calls forth a leucocytosis, and "stimulates the cellular elements of the reticulo-endothelial system" presumably to phagocytic action.

Serotherapy in septicemia. The serum treatment of staphylococcus and streptococcus blood infections with "immunized" horse serum has been most disappointing. Apparently it is impossible by any method yet known to immunize horses with any of the products of these organisms so as to produce any really protective antibodies, which can be passively transported in the serum to the patient and which will effectively control the spread of the infection. Recently, however, Cadham (2) has briefly presented a series of 95 cases of hemolytic streptococcus and staphylococcus-aureus septicemia with only 10 deaths, as compared with a previous mortality in similar cases in his hospital of 85 per cent. These patients were treated with rabbit serum prepared in the following manner:

Six-months old rabbits receive semi-weekly injections of different vaccines prepared from septicemic strains of both hemolytic streptococcus and staphylococcus aureus. When they are two years old they are ready for use. A series of 25 rabbits is kept thus prepared and always ready. Whenever a case of septicemia comes into the hospital, the organism is obtained from the blood, and a vaccine is made. This is injected into each of a series of several of the prepared rabbits. After twenty-four hours from 6 to 10 c.cm. of blood are drawn from the heart of 1 rabbit, the serum is removed, tested for sterility, and injected subcutaneously or intramuscularly into the patient. At the same time the serum from 60 to 100 c.cm. of blood of a compatible donor is obtained and injected. The rabbits continue to receive the patient's vaccine, and each yields in turn 6 to 10 c.cm. of heart blood, the serum of which is given to the patient. The average number of these combined injections is four and the most ten. Cad-

ham is of the opinion that the rabbits prepared by preliminary injections very rapidly produce a potent antiserum containing antibodies, for which the additional human serum yields complement. If these remarkable results can be confirmed, there is hope for future success in this field.

Lyons (13) has recently suggested the possibility of stimulating antibacterial as well as antitoxic substances against the staphylococcus aureus by the injection of vaccine made from very young capsulated forms. Whether or not this procedure will be able to increase the potency of serum, further laboratory and clinical experience will have to determine. The injection of similar vaccine into patients who are suffering from a prolonged septicemia has also been suggested. Likewise an attempt has been made by Bergey and his associates (1) to stimulate the production of staphylococcus antitoxin in blood donors by the intracutaneous injection of increasing concentrations of toxin until there is no longer any skin reaction to the undiluted material. When the reaction no longer occurs they believe it is indicated that the donor has developed antitoxin and that his serum will be efficacious when given to a patient with staphylococcus septicemia. In some cases they also have thought that they were able to develop a potent antitoxin in the patient during the course of the infection by a similar series of intracutaneous injections of toxin.

Transfusion of blood in surgical septicemias. Kolmer (11), Unger (23), Stetson (22), and others all favor the frequent administration of small transfusions in cases of septicemia. They claim, quite without clear proof of their existence, that immune substances are thus transferred from the donor to the patient. Stetson's figures of 10 deaths in 19 cases of hemolytic streptococcus septicemia and 9 deaths in 12 patients with staphylococcus-aureus septicemia are not particularly convincing as to its efficacy. Unger reported only 9 recoveries in 42 cases of septicemia treated with repeated direct transfusions from normal donors and attempted to improve these figures by "immunizing" his donors by the injection of the homologous or heterologous strains of organisms. However, his recoveries were not materially increased thereby and frequently the donors showed no evidence of having developed any immune substances. Almroth Wright (24) was not satisfied with the results of ordinary transfusion and proposed his "non-specific immunotransfusion," prepared by the addition of certain non-specific vaccines to the blood *in vitro* before its administration. A number of other workers have followed this suggestion with variable success. Crocker, Valentine, and Brody (5) express their own feeling with regard to it by saying that "unless there is adequate natural or surgically established drainage of the foci of infection, the beneficial effect of the non-specific immunotransfusions is only transitory."

Recent work by Lyons (14) indicates perhaps why it is that occasionally brilliant results are obtained by transfusion in cases of hemolytic streptococcus septicemia. He has been able to determine by a special technique that about 1 donor in 10 or 20 will have potent natural opsonins for the patient's organism and the donor's leucocytes will show a high degree of phagocytic power. He claims that a selection of such a donor will yield much more benefit than the blood of the average donor or of one who has been artificially immunized. The difficulties of obtaining a large number of donors to test for each case and the exact requirements of the technique render this method of selecting the donor impossible in most institutions at the present time. The method has not been applied to other types of septicemia as far as I know.

Even though, from an immunological standpoint, transfusion is not what its chief advocates would have us believe, it has its indications in cases in which there is a real reduction of red cells and hemoglobin. Neuhof (17), Scott (20), and the writer all feel that its chief value lies in this field. Even for this anemia, however, one adequate surgical approach to the distributing focus is worth many transfusions.

For the most part, the evaluation of the reports of chemotherapy, serotherapy, phagotherapy, and transfusion in septicemia is difficult because usually no details of the surgical procedures are given in the cases so treated. It would require a very careful unbiased analysis of each individual case of a large series to weigh and measure the rôle played by any one therapeutic measure. It is generally agreed, however, that the surgical attack on the distributing focus is of prime importance; therefore, I end this paper as it began, by saying that *in a case of septicemia due to pyogenic or necrotizing organisms it is the surgeon's responsibility to locate the distributing focus and, if possible, to remove, drain, or isolate it.* The present high mortality of septicemia is a challenge to our profession.

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TUMORS OF THE MOUTH AND JAWS

Collective Review

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FOREWORD

THE oncologist is confronted with a very complex problem when attempting to classify oral tumors. A large number of tumors arise from the soft tissues of the oral cavity or the neighboring glands, some form from the cellular elements of the jaws, while still others originate from enclaved cell rests of the embryonic chondroskeleton, or structures derived from tooth formation.

In my text, *Clinical Pathology of the Jaws* (107), I have adapted for the tumors of the mouth and jaws the simplified classification established by the Registry of Bone Sarcoma for bone tumors in general, and except for minor changes this classification has been very satisfactory. It will serve me to discuss the collected material for this review in a comprehensive manner.

I. TUMORS OF OSTEOGENIC ORIGIN

Osteogenic tumors of the jaws, like those of the rest of the skeleton, are derived from osteogenic tissue, that is, cells and ancestors of cells which, when fully differentiated, are known as osteoblasts. Slowly growing benign tumors generally are made up of cells all showing the same stage of development, so the pure myxoma, chondroma, and osteoma result.

Two cases of myxoma are reported, one by the New York Institute of Clinical Oral Pathology (70) and the other by Salama of England (89). The first occurred in a woman aged twenty-five who complained of a dull pain in the region of the right maxillary first molar. A swelling of 1½ cm. in diameter could be seen bulging buccally. On x-ray examination a honey-combed osteolytic change was noticed which was not diagnostic; giant-cell tumor, polycystic adamantinoma, osteitis fibrosa, myxoma, and central fibroma were considered. At operation the lesion was found to extend into the molar process and to be made up of a yellowish-white tissue which on microscopic examination showed a pure myxoma replacing the spongiosa of the alveolar bone completely. The second case involved one side of the mandible of a man aged twenty-seven. It was associated with a painful tooth which was exfoliated. The x-ray showed a diffuse bony rarefaction of the honeycomb type in the horizontal and ascending ramus, which on microscopic examination was found to be due to osteoclastic resorption of bone caused by a fibroma in which marked myxomatous changes were seen. The right mandible was excised.

Chondromas, although not uncommon, were not reported this year. Several articles dealing with various forms of osteoma have been published.

Multiple osteomas. Osteomas may occur in multiple form. Ehrenfried (1917) described a hereditary deforming chondroplasia with multiple exostoses, of which about 600 cases have been reported, 2 or 3 affecting the skull. A case of multiple osteomas involving several bones of the skeleton was recently described by Fennel (24) of Honolulu; his patient was known as "Knobby Willy" or the "exostotic kid." This case is of special interest because, although the patient had had these exostoses ever since he could remember, one developed into osteogenic sarcoma at the age of forty-five. A case of multiple mesenchymal tumors, mostly osteomas, involving principally the skull has been published by Thoma (112). The patient aged eighteen, of Italian descent, complained of pressure against his ear when opening his jaw. This was due to a large osteoma attached to the ramus of the mandible near the neck of the condyle. Other osteomas were attached to the mastoid process, several to the lower border of the mandible on each side, and one occupied a large part of the right maxillary sinus. Pathological examination of the excised eburnated odontomas showed them to belong to the classification of osteoma durum.

Osteoma. Solitary osteomas may be made up of compact bone (osteoma durum) or may contain a spongiosa in the center (osteoma spongiosum); they may be peripheral or central in location. A special form of osteoma is the torus palatinus which develops on the roof of the mouth (Fig. 1). It is looked on by some as an exostosis because it develops as two bony outgrowths at the median

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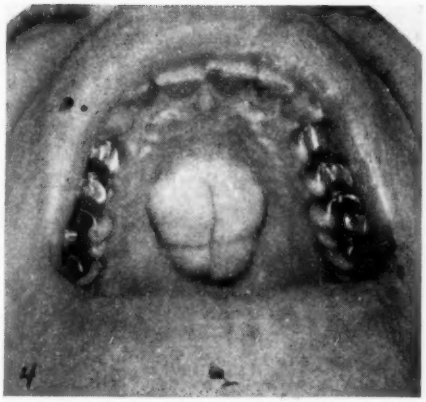

Fig. 1. Torus palatinus. The tumor has developed slowly over a period of many years. (From Internat. J. Orthodont., & Oral Surg., 1937, 23:194.)

line of the hard palate. When expanding these growths form a lobular, pedunculated tumor covered by mucosa, which in some form or other is seen in from 5 to 10 per cent of all white adults. Thoma (113) has written an article describing the development of this tumor, which when very large interferes with eating and speech, and hinders the construction of a well fitting denture. Several types are illustrated and the technique of excision is described.

Fibro-osteoma. This is a benign osteogenic tumor. It has heretofore been described under the name of osteofibroma, ossifying fibroma, localized osteitis fibrosa, and localized osteodystrophia. It is a slow-growing tumor, which transforms the spongiosa, expands the bone, causes facial deformity, and changes the architectural arrangement of the bone trabeculæ. The marrow becomes fibrous and shows evidence of cellular activity. It often occurs in the second or third decade of life, and deformity or asymmetry of the face is a prominent complaint of the patient.

Thoma (116) distinguishes the following types:

1. Ossifying fibroma in which the fibrous tissue is formed in excess and bone trabeculæ are rare. [Example: Phemister and Grimson (74), Fig. 31.]

2. Fibro-osteoma in which the spongiosa is represented by well calcified irregular bone trabeculæ, and the marrow spaces are filled with fibrous tissue often containing some osteoclasts, besides active osteoblasts in very large numbers. This is the common type.

a. Fibro-osteoid-osteoma in which the newly formed bone trabeculæ are poorly calcified (Figs. 2 and 3).

Fig. 2. Fibro-osteoid osteoma. Roentgen picture of a girl aged sixteen, showing radiopacity of maxillary sinus extending into the malar bone. (From J. Am. Dent. A., 1938, 25:750.)

b. Fibrosclerosing osteoma in which well calcified bone is formed in excess and fibrous marrow is very scarce. [Example: Thoma (116) Fig. 20.]

Worth (123) distinguishes three types which he describes under the name of localized osteitis fibrosa. The most common type, he writes, is found usually in the maxilla of young patients and results in swelling of the molar and premolar regions. In the roentgenogram the newly formed bone has a homogeneous density and presents a stippled appearance. At operation it is found to be quite soft and easily removed. The reviewer classifies this type as fibro-osteoid-osteoma. Another type, occurring in older patients, resembles a mass of new bone arising from the alveolar border of the maxilla, extending downward, and interfering with the closing of the mouth. The bone is dense and rather structureless, hard at operation, and radiopaque in x-ray examination. The third type occurs in the mandible which shows considerable increase in depth of the bone, and in the roentgen picture varies a good deal from the "ground glass" to the "granular" or stippled appearance. There may or may not be areas of rarefaction present. It is usually found to be hard at operation.

Phemister and Grimson of Chicago (74) reported 13 cases in an article already reviewed (9a). They observed that the tumors are slow-

growing, and when starting in childhood tend to become stationary in adult life. They state that the lesion appears to be a true neoplasm and not a form of osteitis fibrosa, hyperostosis, or chronic inflammation. In 3 of their cases it consisted largely of fibrous tissue in various degrees of maturation with ossification proceeding slowly. In 12, the tumor consisted largely of cancellous bone and fibrous marrow. There was myxomatous tissue present in 3, and occasional small islands rich in giant cells in 2. No case showed evidence of malignancy.

Charbonnel and Massé (15) reported 1 case, and Gullifer of Boston (35), in an article dealing with this type of tumor, showed illustrations of 3 cases, 2 of the maxilla, and 1 with lesions in the mandible; all were of the fibro-osteoma type, but were listed as localized osteitis fibrosa.

According to the reported cases the disease is more common in the maxilla than the mandible, occasionally occurs in both maxilla and mandible (Phemister and Grimson), and may form multiple lesions in one bone (Gullifer). In the upper jaw the disease may be limited to the anterior part, or the tuberosity, but there is a typical lesion which obliterates the maxillary sinus, causes expansion of the bone in the canine fossa, and invades and expands the malar bone. The lower border of the orbit may be thickened and the eye pushed to a higher level. Such a case is well illustrated in Thoma's article (116), Figures 16 and 17. The palate may bulge into the mouth in very extensive cases, as shown in Figure 4 of Phemister and Grimson's article (74). The nose is not involved, which is of importance in differentiating diagnostically from the diffuse hyperostoses and leontiasis ossea, in which obliteration of the nasal meatus is an early symptom. In the lower jaw expansion of the bone without definite demarcation is an early roentgen sign. Differentiation from osteogenic or other cysts presents no special difficulty because in fibro-osteoma there is no parchment-like condition of the swelling, and the x-rays do not show the well defined cystic margin; but thinning out of the cortex, distortion of the mandibular canal [Thoma (116) Figs. 10 and 14], and obliteration of the outline of the maxillary sinus are characteristic signs. There is no periosteal bone formation. In some roentgen pictures, the spongiosa is so changed that a typical stippling may be seen, which reminds one of the texture of an orange peel [Worth, (123), Fig. 18]. The relation of the teeth to the tumor plays no direct part in the disease. Trauma, caries of the teeth, and extraction or other infections are mentioned in the history of most cases.

The blood calcium and phosphorus are generally normal and the disease, though often termed localized osteitis fibrosa, is not in any way related to generalized osteitis fibrosa of the hyperparathyroid type, Paget's disease, or benign giant-cell tumor. The histological picture shows a great variation in the amount of fibrous and osseous tissue. Some cases show areas of myxomatous change and the presence of foreign-body giant cells. There is no round-cell inflammatory infiltration except in cases complicated by dental infection.

The prognosis generally is favorable; no cases have been reported which have undergone sarcomatous changes. The growth is usually slow, there is no enlargement of the lymph glands, and the general health of the patient is good. The tumor, generally not being circumscribed, is not always completely removed and therefore shows the tendency to recur.

Treatment should be conservative, except in early circumscribed cases when the total excision is possible. In diffuse involvement of the bone when large parts of the jaw are involved conservative operation is advised. The authors referred to agree with earlier writers on the subject (Hippel, Blum, Furedy) that massive resection with its disfiguring results is not justified. Biopsy should be performed to establish definitely the benign nature of the disease. The operation should consist of removing as much of the tumor as possible without running the risk of a poor esthetic result. This is followed by moderate irradiation, up to 3,000 roentgen units, in order to control portions of the tumor not removed at operation. In spite of this the tumor may continue to grow and require a secondary operation later, or finally complete resection.

Osteogenic sarcoma. No reports of osteogenic sarcoma were found in the literature of 1936 and 1937. Two new cases, however, were reported to the Registry of Bone Sarcoma, and kindly placed at my disposal for study. The first, "Case No. 1896," occurred in a woman aged twenty-three, who first discovered a lump on the outside of her right lower jaw. This was hard, fixed, and the size of a marble; it started to grow more rapidly after it was excised. Growth was accelerated by several minor operations, extraction of a tooth, excision of the growth and radium treatment. Roentgen examination showed an expansible type of lesion in the right jaw extending from the region of the first premolar back to the third molar and beyond, and causing an irregularity of the bony trabeculæ. Pathological examination showed dense fibrous tissue enclosing a diffuse

growth of polyhedral-shaped cells without clearly defined cellular limits. Some of these cells appeared to form small lacunar spaces with the nuclei occupying the periphery of the space. This tissue gradually differentiated into cartilaginous tissue. Numerous mitotic figures were present.

The second case, No. 1571, occurred in a man aged twenty-nine. He noticed a lump on the right side of the jaw in the molar area. Two teeth and a retained root had been extracted three or four years before. The lump had gradually become larger. Roentgen examination of the excised right mandible showed a remarkable bony growth extending about 1.5 cm. from the inner and outer side of the mandible and from the lower border. This new bone was laid down in striæ perpendicular to the shaft, producing in the roentgenogram the characteristic sun-ray effect of osteogenic sarcoma. There were also shown marked malignant changes in the bone, and roentgen examination of the face revealed metastases to the left side of the maxilla, other bones of the face, and the lungs. Pathological examination showed typical cartilage and osteoid tissue in a matrix of spindle cells varying in size and arrangement and containing numerous mitotic figures. Multinucleated giant cells were frequent. The tumor cells invaded the muscle bundles attached to the jaw. The patient died three months after operation.

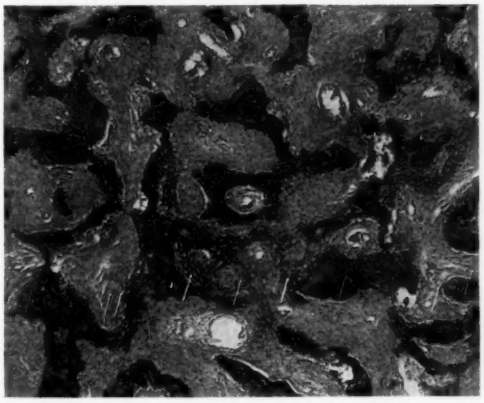

Fig. 3. Fibro-osteoid osteoma. Photomicrograph of bone excised from maxilla of patient shown in Figure 2. (From J. Am. Dent. A. & Dental Cosmos, 1938, 25:750.)

II. TUMORS OF ODONTOGENIC ORIGIN

Odontogenic tumors, derived from tissue of the tooth germ during tooth development or from cellular remnants retained in the jaw, are very common, and a great many articles are at hand which deal specifically with these tumors. Odontogenic tumors may involve only the dental epithelium, when follicular cysts and adamantinoblastomas result; if the mesenchymal tissue is involved, soft and hard odontomas form.

Follicular Cysts. While the radicular cyst derived from an epitheliated apical granuloma is a lesion of infectious origin, we find more and more statements supporting the contention that the follicular cyst which is derived from enamel-organ epithelium is closely related to the adamantinoblastoma, and therefore should be classified as a tumor. The British writers for a long time have classified cysts as odontomes, which is evidenced in the recent article by Sprawson (100) on odontomes, and another by Worth (123) abstracted in *Surg., Gynec. & Obst.*, 1937, 65: 97. Sprawson states that while chemical irritation of the accumulating cystic fluid may be a prime factor in the proliferation of the epithelial lining of the cyst, this is no argument against its inclusion as a neoplasm since many investigators have shown that pure chemical substances used experimentally produce tumors regarded as true neoplasms, such as sarcoma and carcinoma. The French also classify odontogenic cysts as odontomas; Despons (20), abstracted in *Surg., Gynec. & Obst.*, 1937, 65: 201, for example, points out that parodontal cysts which form at the side of a tooth from the enamel organ or from an epithelial sprout given off from it, behave exactly like tumors, because they have a tendency to develop progressively and produce deformity of neighboring cavities. He also points out that such cysts may become multilocular and have the tendency to recur after incomplete operation, because of proliferations which enter the adjoining bone.

The German point of view is stated in an analysis by Hauenstein (38) based on a study of the vast material at the University clinic in Leipzig. Hauenstein describes 16 selected cases which show that both odontogenic cysts and adamantinoblastomas form from the primitive oral epithelium and are therefore closely related to each other. Variations in tumor formation, he concludes, are due to the degree to which the parental cells have differentiated, which explains why many borderline cases occur that cannot be easily classified.

Since Cahn of New York (13) published his article, *The Dentigerous Cyst as a Potential Adamantinoma*, in 1933, more cases showing the transition of an odontogenic cyst to an adamantinoblastoma have been reported. Thoma and Carpenter of Boston (118) reported a case in which small cystic areas were found at the periph-

ery of an odontogenic cyst. On pathological examination some contained small cyst membranes while others contained adamantinoblastoma follicles. Thoma and Proctor (119) also reported a case of a mandibular cyst which after excision was found to present mural thickenings in which an adamantinoblastoma was found to be developing.

Maccaferri (56) who reports on 32 cases of follicular cysts treated at the clinic for mouth disease at Bologna gives the following statistical information regarding relative occurrence: 20 cases were found in the mandible, 12 in the maxilla; 10 cysts originating from the third molar (6 maxillary, 4 mandibular), 11 from the canine teeth (8 maxillary, 3 mandibular), 7 from premolars (3 maxillary, 4 mandibular), 3 from supernumerary teeth, and 1 from an incisor. The writer stresses the importance of determining whether the cyst is infected.

Clinical symptoms in some cases are absent. Facial deformity or nerve symptoms may be complained of by the patient. Piquet and Decoulx of Paris (77) report a case of dentigerous cyst in the anterior part of the mandible in a twenty-nine-year-old patient, which caused headaches over a period of twenty years. To cure these frontal headaches the tonsils were removed and treatment was given for a suppurative otitis media. Blood examinations and lumbar punctures gave no clue to the condition. Only later when x-ray pictures were made of the sinuses was a cyst discovered in the lower jaw. Excision resulted in complete relief of the pain that had persisted for so many years. Lehmann (53) describes similar cases with pains in the back and left side of the head of many years' duration, due to large mandibular cysts. The pains were completely relieved two months after operation.

Grandi (34) states that large cysts of the mandible may cause paresthesia. This is due to pressure and not to destruction of the inferior alveolar nerve, except in cases of pathological fracture when the nerve and vessels may be torn. In such cases the teeth lose their sensory supply, but do not lose the blood supply because of collateral circulation. Grandi recommends careful dissection of the cyst membrane to prevent injury to the nerve.

Deformity due to follicular cyst is not so common because expansion of the cyst occurs first inside the bone. Very large cysts, however, may produce an asymmetrical swelling of the face. Such a case was reported by Bloom of Taiyuanfu (10), who excised a dentigerous cyst in a Chinese woman aged nineteen, which occurred in the maxillary sinus, expanded the bone, extended to the floor of the orbit and the wall of the right nasal cavity, displaced the septum, and caused a bulging of the right half of the palate. It contained 100 c.cm. of clear fluid with cholesterin crystals. The tooth found in and probably causing the cyst was located below the infra-orbital margin.

Rosedale and Koepf, Buffalo, (86) describe other interesting cases affecting the maxilla, stating that the cysts may perforate the outer cortical plate in the canine fossa and cause bulging of the upper lip, and may extend into the opposite maxilla through the anterior alveolar process and the palate. Cysts located in the hard palate may cause elevation of the floor of the nose and erosion of the palatal plate, which then presents a boggy fluctuant mass. Encroachment on the maxillary sinus causes displacement of the naso-antral wall medially, and in such cases the cyst may obliterate the sinus.

Infection may complicate the picture. Rosedale and Koepf report 3 follicular cysts which became infected. They were painful, and 1 had a history of several exacerbations. Pus escaped when the swelling was incised. In a colored man aged thirty-four the condition was accompanied by fever of 99.4° F. The white blood count was 11,200.

The differential diagnosis between follicular cyst and adamantinoma is not always easy. When the roentgen film shows a monocystic defect, diagnosis of follicular cyst is not certain, even though the cyst contains a tooth (dentigerous cyst). This is brought out in an article by Oesterreich (71), who points out that 3 cases roentgenographically diagnosed as cysts proved on histological examination to be adamantinomas. Jacobs (45) described such a case, and I have received 2 cases this year for pathological examination, which in the roentgen picture could be diagnosed as dentigerous cysts, but which proved to be monocystic adamantinomas. Fig. 4 shows the roentgenogram of one of these cases referred to me by Dr. Hyde of Brooklyn, New York, for diagnosis. The photomicrograph, Fig. 5, shows the pathology, a solid adamantinoblastoma.

Schupfer (92) recommends puncture of the cyst, withdrawal of the cyst fluid by means of a syringe, and replacement of the fluid by a radiopaque fluid for the purpose of identification in the x-ray examination. He advises the use of "thorotrast." The aspiration of the cyst fluid is of course a well recognized procedure in the differential diagnosis of cysts; the use of a radiopaque substance for injection into the cyst lumen often gives valuable information regarding the size and

Fig. 4. Monocystic adamantinoblastoma (W. H. Hyde). Roentgen picture shows cystic area in ramus adjacent to third molar, from the epithelial organ of which the tumor must have formed.

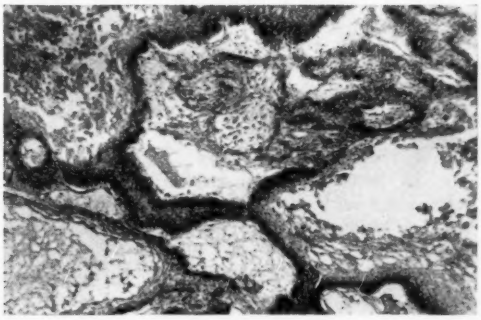

Fig. 5. Monocystic adamantinoblastoma, photomicrograph of case shown in Figure 4.

outline of the lesion. This is of importance especially in the maxilla where the septa of the maxillary sinus are often mistaken for the walls of a cyst. I (117) have recommended the use of lipiodol for this purpose and found it a great help in difficult cases.

Other cystic lesions must be differentiated, such as, first of all, the traumatic cyst which occurs in adolescence from trauma insufficient to cause fracture but producing intra-osseous hemorrhage. Such cysts have been described by Ivy and Curtis of Philadelphia (42) and by Smith and Barrows of Providence (99). Another cyst which gives difficulty in diagnosis is the facial cleft or fissural cyst caused by enclaved epithelium at the junction of the embryonic facial processes. This has been described by Thoma of Boston (114) and by Stafne, Austin, and Gardner (103) who point out that when large it may be difficult to distinguish it from an odontogenic cyst. The incisive canal cyst may also attain large size, when it is difficult to differentiate it from cysts of dental origin, as demonstrated by a case reported by Cohen and Levine of Boston (17).

In treatment of follicular cysts complete excision of the cyst sac is advised, as the tissue must be considered a potential adamantinoblastoma. Leo Winter (122) in an article on cysts of the jaws discusses the methods of treatment and stresses the importance of differential diagnosis of cysts and adamantinoma, particularly in cases of multilocular tumors. He recommends complete enucleation of the cyst. For large cysts of the upper jaw encroaching upon the maxillary sinus Schupfer (93) prefers the rhinological approach because little after-treatment is necessary, a large oral opening into the cyst, such as results from the Partsch operation, is avoided, and the early replacement of teeth by means of a denture is possible. I, personally, prefer excision of the cyst sac by means of an oral operation, removal of the bony partition separating the cyst from the sinus, and, if there is no infection present, closure of the oral opening by means of a large and liberal palatal mucosa flap. Rosedale and Koepf (86) advise the same treatment with a large-sized window under the inferior turbinate to connect the cystic cavity with the nose and establish adequate drainage. This procedure is indicated particularly in case of infected uninvolved parts of the maxillary sinus. The window also facilitates irrigation.

Wuest (124) in a dissertation on mandibular cysts states that in cases of large cysts there is danger of fracture of the jaw, as it is difficult to determine its thickness with the x-rays. He recommends the use of a splint constructed and applied to the teeth previous to the operation. The spontaneous cure of a cystic tumor in the mandible after extraction of a tooth is reported by Lafite-Dupont (51). The patient, sixty-eight years old, presented a carious aching mandibular six-year molar which was extracted. The so-called cyst, however, was a gingival swelling of the size of a small walnut, no doubt a chronic inflammatory periosteal swelling rather than a true bone cyst.

Maccaferri (57) reports a case with two dentigerous cysts in which the teeth (six-year molars) erupted within a year after operation. The cyst sac was excised according to the method of

Sprawson, the teeth being left in position. Such a case was also reported by Thoma (108), and operated upon in a similar manner with excellent results. Maccaferri recommends this procedure for the treatment of dentigerous cysts in the following cases:

1. If the cysts are still small.
2. If the cyst is in the alveolar process close to the surface, and if the involved tooth is not greatly transposed and has roots that are well developed.
3. If the affected person is young.
4. If the cyst is not infected.

Matolessy (63) of Budapest recommends for large cysts the use of a tibial bone graft transplanted with periosteum to obliterate more rapidly the cystic cavity. Of 45 cases, 43 healed by primary intention; in 2 the transplant was expelled. The follow-up roentgen examination showed that in young patients the transplant was rebuilt into the jaw in from eight to ten months, while in older patients it took as much as three years. One of the advantages of this procedure is the protection of the jaw against fracture.

Multiple follicular cysts. Follicular cysts are quite often found in multiple form. A large number of cysts may develop in one place from one anlage. Such cases are quite common. Harpole of Atlanta, Georgia (37) reported several unusual cysts and described one of this type. It was a dentigerous cyst which occurred in a female negro aged twenty-six and involved the third molar. It was multilocular in type and spread from the third molar region into the ramus.

Less common are multiple cysts in one jaw or in both jaws, formed in various locations each from a separate anlage. Such cases represent a predisposition to cyst formation, which may be due to genetic factors. Maccaferri (57) reported a case of bilateral cysts in a boy aged seven. They were dentigerous cysts formed by the first mandibular molars. Seeman of Nashville, Tennessee, (94) treated a male patient, aged sixteen, with two maxillary and two mandibular cysts. They were dentigerous, one containing a third molar, the other three each a second and third molar. Bennett of Tucson, Arizona, (7) describes a similar case but of more extensive involvement. Cysts were found by roentgen diagnosis as follows: (1) dentigerous cyst from the left maxillary cuspid; (2) dentigerous cyst from the right maxillary cuspid; (3) cyst involving the antrum from a molar tooth; (4) cyst involving the anterior part of the mandible, extending from the second molar on the right around the symphysis to the first molar on the left and containing a retained incisor; and (5) cyst at the angle of the jaw involving half the ramus and the third molar. Physical examination was essentially negative; the cysts were excised at different times. Worth (123) points out that in some cases there is a familial tendency to the production of odontogenic cysts.

What might be called "cystomatosis" is a condition which has been described by Jones of Kingston, Ontario, Canada, (47) under the title, *A Case of Familial Multilocular Cystic Disease.* The patients observed by Jones were 4 of 5 children of a Hebrew family, descendants from Russian immigrants. The disease set in after the second year of life and caused a bilateral painless swelling of both upper and lower jaws, accompanied by a chronic hyperplastic disorder of the submaxillary and cervical lymph glands. The protuberance of the cheeks and jaws and upward turning of the eyes associated with it gave the children a cherubic appearance which prompted Jones to coin the word "cherubism" to describe the facies produced by the disorder. The disease is caused by a polycystic condition involving both the upper and lower jaws completely. As some of the patients were under observation for six years it was possible to demonstrate by means of roentgen examination the progressive enlargement of the cyst causing marked expansion of the bones. A more complete abstract of this case has been printed in an issue of this journal (*Surg., Gynec. & Obst.*, 1938, 67: 219).

Jones also cites another case, the description of which was put at his disposal by P. J. Thomas of Savannah, Georgia. The cyst occurred in a boy aged eleven and caused a similar disorder of both jaws, but did not involve the lymph glands. It showed, however, a marked hereditary characteristic, a similar type of cyst having occurred through five generations. A genetic chart is included. There was no pathological examination of these cysts and the diagnosis was based on the roentgen findings. Other probable diagnoses mentioned by the writer cannot therefore be excluded definitely; the diagnoses under consideration were cystic adamantinoma and fibrocystic disease of the jaws. It is interesting to know that a case of similar roentgen appearance has been reported by Salama of England (89). The growth involved only one side of the mandible and ramus, the maxilla being normal. It was reported as a case of multilocular cyst, and a third molar was found in the ramus near the mandibular notch. A microscopic examination was made, however, both before and after the operation and the final diagnosis was fibroma with marked myxomatous changes.

Adamantinoblastoma. The adamantinoblastoma forms either directly from the epithelium of the enamel organ, or indirectly from the oral epithelium, from remnants of the dental lamina, or from follicular cysts. It never produces calcified tissue and for this reason the name adamantinoma is somewhat misleading. It may produce a monocystic bone lesion or a polycystic tumor. Monocystic tumors resembling follicular or dentigerous cysts have already been mentioned, and so have odontogenic cysts, which on microscopic examination showed the formation of an adamantinoblastoma in the cyst sac. Such cysts may ultimately become filled with tumor tissue and become solid adamantinoblastomas or, if the epithelium proliferates peripherally, they may form multilocular tumors.

Ivy and Curtis of Philadelphia (43) quote Churchill (16) who pointed out that in microscopic diagnosis of follicular cysts proliferating epithelium may be seen surrounding islands of connective tissue; these are pseudofollicles and the cyst membranes containing them are not potential adamantinomas. It is important to differentiate such structures from true follicles, which contain stellate epithelial cells and no blood capillaries such as are seen in connective tissue. The writers of the article, however, point out that the clinical course of the aberrant follicular cyst resembles very closely that of the adamantinoblastoma and therefore for practical purposes the treatment is the same. Kotany (50) of Vienna describes a very small cyst situated between the mandibular second premolar and the first molar of a girl aged nineteen, which on microscopic examination was found to be an adamantinoma. He stresses the importance of having a microscopic examination made of all cystic membranes.

Hauenstein of Leipzig (38), in an excellent article, describes a number of cases which demonstrate the importance of histological examination. Two dentigerous cysts which were found to be adamantinomas on microscopic examination are described. In other cases in which the clinical and roentgen diagnosis favored adamantinoblastoma on account of size, shape, and polycystic roentgen appearance of the lesion, the tissue on examination proved the lesion to contain the ordinary epitheliated connective tissue sac of a multilocular follicular cyst. This writer says he disagrees with Axhausen, who demands biopsy examination in all cases of multilocular tumors and advises excision of large pieces of tissue for this purpose. Hauenstein believes in conservative treatment for adamantinoma as well as for cysts and therefore his treatment is essentially the same for both tumors, if they are well encapsulated and can be easily enucleated. The tendency toward recurrence after operation should lead us to excise the tumors carefully and thoroughly rather than influence us to advise radical treatment.

Hauenstein states that careful histological study of the excised tissue is advised because of the many characteristics of this tumor and the changes it may undergo. The fact is stressed that the tumor forms from epithelium, which in its development has many possibilities and may differentiate into glandular as well as dental structures, and even may, though rarely, undergo carcinomatous changes. Robinson (84) made a very careful histological study of 16 cases of ameloblastomas; he preferred this name to adamantinoblastoma. He concludes from his observations that the various stages of development of the enamel organ may be represented up to the point at which the normal ameloblast assumes function. From this point on a divergent development takes place. In the normal enamel organ the cells generate enamel, but in the tumor the ameloblastic follicles degenerate to a non-functional cystic mass. He believes that the solid and cystic adamantinoblastomas represent stages of development rather than distinct types of tumors. A case of adeno-adamantinoblastoma which developed on the lingual side of the ramus as a peripheral tumor without involving the bone is described. It was composed of squamous, glandular, and enamel-organ epithelium. Gullifer of Boston (36) also described a peripheral tumor resembling an adamantinoma histologically. It formed in the submucosa of the gingiva in the anterior part of both maxilla and mandible. An adamantinoblastoma with cavernous hemangioma was reported by Oesterreich of Leipzig (71), who also cites other cases of mistaken diagnosis made by means of clinical and roentgen investigation. On histological examination in 3 cases the cysts proved to be adamantinoblastomas, and in 2 cases the adamantinoma and osteoma, respectively, turned out to be central giant-cell tumors.

The question of malignancy is discussed by Robinson of Buffalo (85), who in reviewing all the reported cases of adamantinoblastoma found a few scattered cases which were suggestive histologically of malignant growth, a metaplasia to sarcoma or carcinoma. Among 379 reported cases 17 presented evidence of malignancy. In 9, metastases which proved to be of adamantinoblastomatous nature were observed. Seven cases were classified by the writer reporting them as (1) sarcoma ameloblasticum, 3 cases; and (2) carcinoma ameloblasticum, 4 cases. This demon-

strates the importance of histological examination which is brought out also by a case report by Hauenstein (38) who describes a new case of the rare combination, adamantinosarcoma. The biopsy examination led to the diagnosis of adamantinoma. The operation was delayed three months by the patient, and when the excised tissue was examined the connective-tissue stroma showed the development of sarcoma.

Clinical data is available in Ivy and Curtis' excellent article already mentioned (42). They describe 16 cases, 7 in males and 9 in females and 11 in white patients and 5 in Negroes; in 15 cases the tumors were located in the mandible and in 1 case in the maxilla. Five of the tumors which were treated by conservative operation recurred.

Robinson (85) also gives carefully compiled data arranged in tabular form of the 379 cases of adamantinoblastoma studied from the literature. The summary of these findings is as follows:

TABLE I.—ADAMANTINOBLASTOMA

		Cases
Total number of cases		379
Sex (311 cases)		
Male	45.7%	142
Female	34.3%	169
Average age at time of report	37.6 yrs.	248
Average duration of tumor	8.5 yrs.	232
Average age at time of discovery	30.1 yrs.	222
Site of growth (293 cases)		
Mandible	83.7%	247
Maxilla	16.3%	48
Structural characteristic (219 cases)		
Cystic	57.5%	124
Cystic and solid	24.2%	53
Solid	19.1%	42
Contained unerupted teeth		14
Enamel pearls, keratinization		16
Recurrence after operation		119
Metastases or histological evidence of malignancy	4.5%	

Dodt of Hamburg (21) reports a case of maxillary adamantinoma which recurred one year after operation, and in seven years developed to tremendous size; it enlarged the right and left cheek, the nose, and the forehead, pushed the eyes sidewise, and caused marked swelling of the palate and epipharynx. The patient presented a monstrous appearance, resembling a hippopotamus.

A very large adamantinoblastoma of the anterior part of the mandible was reported by Jaulain of Bordeaux (46) in a woman aged fifty-two. It had developed for fourteen years, and after an automobile accident causing fracture of the skull and the mandible, the tumor, already the size of a man's fist, tripled and reached the size of the head of a child. While the tumor was painless it interfered greatly with speech, swallowing, and mastication. After one and one-half years the patient finally consented to be operated on. The tumor including the anterior part of the mandible was excised by radical operation. In spite of good early recovery, the patient died of pneumonia on the thirteenth postoperative day.

Adamantinomas occasionally occur in other bones, and in the hypophysis. A case of adamantinoma of the tibia in a woman aged thirty-six was reported by Holden and Gray of Newark, New Jersey, in 1934 (*J. Bone & Joint Surg.*, 1934, 16: 401) and is to be added to a case occurring in a thirty-seven-year-old man reported by Bernard Fischer of Frankfurt, (*Ztschr. f. Path.*, 1913, 12: 422); a case in a forty-six-year-old man was reported by Baker and Hawksley (*Brit. J. Surg.*, 1931, 18: 415); a case in a man aged thirty-six was reported by Ryrie (*Brit. M. J.*, 1932, 2: 1,000); and another case by Richter (*Ztschr. f. Krebsforsch.*, 1930, 32: 273). All authors lay considerable stress on trauma which they believe stimulates a supposed cell-rest into growth.

The treatment of adamantinoma was subjected to considerable discussion in all the articles that were published. Foremost is the question of whether it should consist of curettage or resection. Jaulain (46) states that curettage will preserve the bone and therefore will serve to maintain the support to the soft tissues of the floor of the mouth and produce less deformity. To be efficient, this treatment must remove the entire tumor and the resection should be carried into healthy tissue. The method should be confined to early, small, and localized lesions. Resection carried out in healthy tissue far away from the lesion is advised for extensive tumors, and prevents recurrence. This is a grave operation, Jaulain states, and in spite of all precautions many patients succumb to resulting cellulitis or bronchial pneumonia.

Calvin of St. Paul (14) stresses the fact that most adamantinoblastomas grow slowly and distend the jaw more than destroy it. He reported a case with a long drawn-out history and apparently benign course. Four conservative operations were performed between 1921 and 1929, after which the patient was kept under observation for seven years. During this time there was no evidence of recurrence. Calvin advises careful x-ray study to determine whether it is possible to avoid resection of the jaw. He also advises radical operation without destruction of the continuity of the bone; for example, the lower border of the mandible is to be left to maintain the form and support of the jaw. With this operation recurrences may be avoided or at least long delayed.

Many of the German writers believe in biopsy examination in order that the type of treatment can be determined for each case.

Reinmoeller of Rostock (82) points out that most of the cases described in the literature show a slow gradual development, but that a fairly radical excision performed when the tumor is small may save the patient recurrences, and repeated and more serious operations. He also says that there are cases on record in which the tumor recurred even though radical resection was performed early. In one case the recurrence occurred after forty-three years, in another after forty-five.

Hauenstein believes that a difference should be made in the treatment of well encapsulated tumors, and of those that show malignant tendencies. Lange of Koenigsberg (52) represents the German point of view, championed by Axhausen, who advises careful biopsy examination to indicate the method of treatment. This not only facilitates the establishment of a differential diagnosis from other central tumors of the jaws which may simulate the roentgen appearance of an adamantinoblastoma, but helps to detect malignant tendencies in both the tumor epithelium and the connective-tissue stroma of the latter. The importance of careful differential diagnosis is also pointed out by Kotany (50) of Vienna who represents the school of Pichler. The routine procedure for adamantinoma in the surgical clinic (jaw department) of the University of Vienna is conservative, because of the belief that serious and mutilating operations are only justifiable as a last resort in the treatment of a benign tumor such as adamantinoma. The removal is by thorough curettage followed by repeated exposure to radium and periodic control with x-rays. Ivy and Curtis (42) point out that it is very important for every particle of tumor tissue to be removed, otherwise recurrences will surely follow. In early cases they believe it is sometimes possible to obtain a cure by enucleation, especially if the tumor is small and surrounded by well defined bony walls. However, in such cases recurrences are frequent, and finally a complete resection must be performed to secure a cure. When the tumor is large with irregular extension in the bone and perforation of the cortical plate, they feel that complete resection is indicated as the initial treatment. This has been advocated by Simmons (98) of Boston and Rosenthal (87) of Leipzig. Ivy and Curtis report that of 15 patients in whom the mandible was affected, 3 are believed cured after conservative enucleation, repeated several times in 1 patient; 2 are well after a second enucleation followed by an implantation of radium; 5 are completely cured by initial complete resection; and 5 which had recurrences after conservative operation finally came to radical resection with apparent cure. These writers restored the continuity of the mandible from three to six months after resection of the tumor in several cases by means of a bone graft from the crest of the ilium. Douglas Quick of New York (79) in a recent article recommends prolonged heavy external irradiation followed by conservative surgery and postoperative application of heavily filtered radium.

Soft odontomas. These form if the mesenchymal part of the tooth germ is involved in tumor formation. They form either from the embryonic mesenchymal tissue, the dentine papilla, or the dental follicle, and later from the periodontal membrane. The result is a fibroma-type of lesion which may be spoken of as central fibroma or fibro-odontoma, the name indicating its derivation. It is recognized by the frequent presence of dental epithelium in part of the tumor. The latter is derived from the sheath of Hertwig or its remnants. On the other hand, if the epithelium is adamantinoblastomatic then the term fibro-adamantinoblastoma may be justified. In other soft odontomas the mesenchymal part may take the form of a fibrosarcoma and, if dental epithelium is present, may be spoken of as adamantino-sarcoma, which has already been described.

Nagel (68) points out that soft odontomas are easily mistaken for adamantinomas; histological examination helps to make a differential diagnosis. A soft odontoma attached to a dentigerous cyst was reported by Darlington and Lefkowitz (19).

Hard odontomas. These may be produced by mesenchymal tumors in which dentin or cementum has been formed, and are spoken of as *dentinoma* or *cementoma.* In other cases all calcified and uncalcified tooth tissues are represented, either in a form resembling more or less normal teeth—*compound odontoma*—or in a form which bears no resemblance to the anatomical arrangement of the dental tissue—*complex odontoma.* In addition the odontoma, which is ordinarily encapsulated by fibrous tissue resembling the dental follicle or periodontal membrane, may be contained in a cyst, in the wall of the cyst sac, or it may extend into the lumen of the cyst. This type is spoken of as *cystic odontoma.*

Cementomas have been described by Thoma (116 and 115) who points out that the cementum is a secondary formation in these tumors, and is the by-product of a soft-tissue tumor, the cementoblastoma.

In the growing stage the cellular tissue makes up the predominant part; this decreases in proportion as cementum is formed. When the cellular elements have exhausted their activity they remain as a thin connective-tissue capsule around the calcified tumor. Thoma (115) speaks of:

1. The osteolytic stage when the immature cementoma is made up of cellular tissue; mistaken diagnosis is frequent in this stage as pointed out by earlier investigators (Stafne, 102).

2. The cementoblastic stage in which cementoblasts have started to form cementum that can be demonstrated roentgenographically. In this stage the activity of the cellular tissue governs the size of the tumor.

3. The mature inactive stage with a large calcified mass surrounded by little connective tissue.

Thoma (115) and Sprawson (101) of London point out that the histological picture may present great variations because it must be remembered that, although normally bone and cementum are histologically quite distinct, under abnormal conditions it is sometimes impossible to distinguish between them. In most cases the cementoblastoma produces cementicles which are fused together (Thoma, 115, Fig. 9); in other cases trabeculæ develop and are laid down in lamellar fashion (Thoma, 115, Fig. 12). Occasionally the cementum is so atypical that it is hard to recognize it (Thoma, 116, Fig. 5).

Cementoblastomas have the tendency to occur in multiple form; both the upper and lower jaws may be involved, and often this condition is associated with hypercementosis of the roots of the teeth. Baumann of Freiburg (5) cites cases of symmetrical odontomas from the literature, and Thoma (115) illustrates dental films of a case, by courtesy of H. A. Potts of Chicago, of multiple cementomas, and suggests the name *cementomatosis* for this condition. In this connection we must keep in mind that odontogenic tumors have been developed in albino rats by Burn, Orten, and Smith in New Haven (12) on a mild, chronic Vitamin-A deficiency diet (from 0.7 to 8.0 International Units).

Clinical evidence of the tumor is not common. If large, the jaw may expand. Pickett of England (76) has reported a case of neuralgia caused by a cementoma attached to the apex of the distal root of the right mandibular first molar. The patient, a woman aged thirty-two, had suffered for four years from persistent intermittent pain which was so sudden and irregular in onset that she was unable to make plans for her activities in advance, as she might be in agony any time, from pain in the temporal, parietal, and inframaxillary regions on the right side. Three months after extraction of the tooth and excision of the cementoma there had been no return of the neuralgia.

Treatment is surgical; excision is indicated if the tumor is large and expands the bone, especially if it contains much soft tissue and if there are symptoms that disturb the patient. Small mature tumors should not be disturbed, especially if removal requires the extraction of sound useful teeth. Change to malignancy has not been reported in the case of cementoblastoma.

Complex and compound odontomas, cystic and non-cystic, appear quite frequently in the literature during the period covered by this review. Cases were reported by Sprawson (101), Darlington and Lefkowitz (19), Worth (123), Straith (105), and Corless (18).

Complex odontomas. Worth (123) points out that this tumor can be differentiated from osteoma by the capsule which can be shown by x-ray examination to surround the tumor. A complete tooth may be found underneath the odontoma, which is made up of irregular masses of enamel, dentine, and cementum, and has no regular structure or shape [Worth, (123), Fig. 10]. In Straith's case (105) the odontoma was made up of a retained mandibular third molar around the crown of which fitted an eburnated hard mass of bone and dentine that was transversed by canals containing blood vessels. The case reported by Corless (18) occurred in a patient aged twenty-seven who, while serving on a ship, first noticed a swelling on the face which caused muscular trismus. It subsided after one week and recurred in three months with considerable pain. The roentgen picture showed a calcified tumor, the mesial end of which resembled a tooth, and the whole mass was surrounded by an area of bone rarefaction (infection). It was made up of a mass of enamel, dentine, and follicular infolding which separated the tumor from the tooth.

Compound odontomas. These are made up of a large number of separate pieces which generally resemble large and small teeth of irregular shape. The disclosure of these enables the roentgenologist to make a correct diagnosis. Excellent x-ray illustrations are given in Figures 11, 12, and 13 of the article by Worth (123). In the cystic type there is generally a large area contained in the jaw which on x-ray examination has the appearance of a follicular cyst but may be dentigerous and contain one or more fully developed displaced teeth. It differs from the follicular cyst, as Worth points out, because there are also pieces of tooth substance and denticles contained in the cyst, as shown in his Figures 14 and 15.

Dermoid cysts—teratomas. Rare tumors which reproduce composite structures, or parts of the body in abnormal location, are spoken of as teratomas. Sprawson (101) reproduces an illustration of the famous "Gibbs' case" recorded by Gibbs in 1913 (32), in which on one side of the mandible of a patient a large swelling was found to contain layers of teeth—a teratoma. In ovarian and testicular tumors, or dermoid cysts, teeth and other dermal structures may be found, often contained in bone, and sometimes undergoing caries. Sprawson (101) illustrates a roentgenogram of a pelvis showing two molar teeth in an ovarian dermoid. Thueringer (120) reports a case of dermoid structures in an incipient tumor involving the dental pulp, parodontium, spongiosa of the mandible and mandibular canal, and containing hair and hair follicles in addition to the usual constituents of odontomas.

III. NON-OSTEOGENIC AND NON-ODONTOGENIC TUMORS OF THE JAWS

In this group belong a number of tumors of various histological composition forming from tissue in the jaw that is neither osteogenic nor odontogenic in nature. These may be classified as follows: (1) The central giant-cell tumor which expands the bone and is coarsely trabeculated; (2) the central fibroma and fibrosarcoma which produce osteolytic defects, the first circumscribed, the latter of infiltrating character; (3) neurogenic tumors formed from nerve tissue; (4) the central angioma which is very rare; (5) Ewing's tumor which develops in the cortex and involves the bone both centrally and peripherally; (6) multiple myeloma which forms many punched-out areas in regions where red marrow remains in the adult; (7) the central mixed tumor which is definitely cystic in type; and (8) metastatic tumors.

Central type of benign giant-cell tumor. This tumor, looked at by some as a lesion produced by "reactive resorption" or "resorptive new-formation," must first of all be differentiated from the osteoclastoma or giant-cell tumor occurring in generalized osteitis fibrosa of hyperparathyroid origin. A case of the latter type is reported by the Institute of Clinical Oral Pathology (41). It occurred in the mandible of a woman aged forty. A biopsy of the tumor was taken, and it was diagnosed as a benign giant-cell tumor and excised. It recurred in a different location (ramus), and the patient has suffered two pathological fractures in the long bones since the operation on the jaw. Blood chemistry was then advised which showed the blood calcium to be 11.6 mgm. per 100 c.cm., the phosphorus 2.86 mgm. per 100 c.cm. and the phosphatase considerably increased. X-ray examination showed cystic defects in several bones. This is another case added to the list of hyperparathyroid cases which were first seen by the oral surgeon for treatment of a jaw lesion.

Seldin and Darlington (95) point out that the contention of Geschickter and Copeland (28), expressed in their valuable book, *Tumors of the Bone,* is well supported by clinical observations and facts. According to their analysis, the following factors deserve attention and may lead to a better comprehension of the pathogenesis of these lesions:

1. Giant-cell tumors are the result of abnormal hyperplasia of osteoclasts.

2. In giant-cell tumors this osteoclastic proliferation takes place as a phase in the histogenesis of intracartilaginous bone.

3. Histologically the reaction can be divided into (a) an active progressive osteoclasia and (b) a regressive osteoclasia. In the former, hemorrhage and giant cells predominate. In the latter, cystic bone conditions and fibro-osteosis are predominant.

4. Regarding behavior and treatment it may be said that these tumors are benign, their rate of growth is variable, and if they are not thoroughly removed they may recur.

The pathogenesis is discussed by Gullifer (35) who points out that in the jaws these tumors, which he believes to be a reaction to inflammatory stimulus, are found in areas in which, or near which, there are cartilaginous remnants, such as the symphysis mentis, the posterior body of the mandible, and the region of the inferior turbinate in the upper jaw. Other cases of solitary benign giant-cell tumor cannot be attributed directly to precartilaginous ossification.

Symptoms, Major (58) points out, occur in sequence as follows: trauma, pain, tumor, and fracture. His case involved the maxillary sinus in a girl aged nineteen years; the tumor caused marked bulging of the bone. In a case reported by the New York Institute of Clinical Oral Pathology (70), the location of the lesion, which was monocystic, was in the canine and premolar region of the left mandible. Pulp tests were made and it was found that all the teeth involved reacted normally. Gullifer's case (35) involved the same area. It occurred in a boy aged eighteen and showed a trabeculated cyst in the roentgenogram. Seldin and Darlington's three cases were: (1) a tumor in the anterior part of the mandible from the right premolar to the left molar region, causing marked expansion of the bone and perforation of

the cortex, in a girl aged fifteen years; (2) a tumor causing a multicystic swelling of the palate and labial part of the maxilla in a woman aged fifty; and (3) a tumor in a young man aged eighteen years presenting a swelling of the left side of the mandible from the symphysis to the angle, with a multicystic change in the bone and expansion of the cortex.

Several case histories show evidence of mistaken diagnosis and treatment. Differential diagnosis must be made from odontogenic cyst and fibro-osteosis. The roentgenogram, Major (58) points out, generally shows a lobulated cystic area with incomplete trabeculation at the periphery, but as shown by the cases of Darlington and Seldin (95), the tumor may be multilocular and the diagnosis can often be made only by biopsy. Major says also that biopsy must always be done, preferably with the high-frequency current, prior to operation.

Treatment, according to all the writers mentioned, consists of curettage followed either by chemical or thermal (high-frequency) cauterization of the tumor-bearing area. Some surgeons advise post operative x-ray irradiations, but not irradiation without surgery. Douglas Quick (79), however, states that surgery is usually contraindicated in true giant-cell tumor because of the rather unusual response to external irradiation alone, although the response to external irradiation of moderate intensity in these cases is not so spectacular as with this type of tumor in the long bones of the extremities. Seldin and Darlington (95) state that the more vascular the growth the more the tendency toward malignancy and that tumors with small cells are more malignant than those with large ones. The giant cells are of the foreign-body type and not tumor giant cells.

Central fibroma and fibrosarcoma. These tumors develop from non-osteogenic tissues of the bones, according to Geschickter, and therefore should not be classified with osteogenic tumors. The Registry of Bone Sarcoma, however, classifies central fibrosarcoma as osteogenic sarcoma. A tumor of this type in the mandible of a woman aged thirty-eight is reported as their Case No. 1,362.

Central fibromas are generally formed from the embryonic connective tissue of the tooth germ, dental follicle, or periodontal membrane, and often contain dental epithelium, when they are classified as fibro-odontoma or soft odontoma (see above). Other central fibromas form from the perineural sheath and are generally classified as perineural fibromas. I have 2 such cases in my collection (see neurogenic tumors). Finally, central fibromas may form from retained embryonic connective-tissue cells, and in this connection the pathogenesis of the ossifying fibroma should be kept in mind (see above).

Central fibrosarcoma must be differentiated from peripheral fibrosarcoma arising from the periosteum of the bone. Kitchen and Doan (49) state that a loose tooth, or several loose teeth, is the common first complaint in these cases, and therefore extraction of the tooth or teeth is often performed without recognition of the true condition. It was Bloodgood who pointed out some years ago the value of the roentgen picture as an aid in differential diagnosis in such cases. If a lesion is revealed which differs in any respect from the ordinary root abscess, one should not extract the tooth unless one is prepared to make a frozen section from material that can be scraped from the tooth. Preservation of life may depend on the first treatment when a central tumor of the jaw is exposed.

A case is reported by Kitchen and Doan (49) which occurred in a young man aged eighteen, who had had the mandibular second premolar removed by a dentist a month ago. When the swelling persisted and the first molar became loose, this tooth was extracted also. In both sockets an excessive growth developed which appeared as a roughened, grayish-pink granulation-like tissue. There was marked swelling over the region of the mental foramen, and the roentgenogram showed enlargement of the mandibular canal and "multiple sarcomatous lesion of the mandible." Biopsy showed a cellular tumor growth diagnosed as round-cell sarcoma. The patient received deep x-ray therapy, but in spite of noticeable resorption and disappearance of the initial lesion, there were recurrences involving the other side of the mandible, the left and right maxilla, the right mastoid region, and the right temporal region. All the teeth in the involved areas of the jaws became loose, and the patient died from general metastases four months after the first tooth extraction. Biopsy of metastases taken from the groin demonstrated round-cell sarcoma.

Neurogenic tumors. These tumors are formed from nerve tissue and are very rare. I have 3 cases in my collection. One is a fibroneuroma; another an amputation neuroma occurring in the mandible after evulsion of the inferior alveolar nerve for treatment of tic douloureux, which contained ganglion cells [Thoma (107) Fig. 242]; and a perineural fibroma. It is very interesting therefore to find a new case in the current literature.

This case is reported by Zilkens (125) and occurred in a boy aged seventeen. He had had a swelling of the chin for eleven years, which was a

tumefaction the size of a walnut, covered with natural skin. Intra-orally it presented a swelling the size of a pigeon's egg covered with normal mucosa, and no permanent teeth had formed in this region. Follicular cyst was suspected and seemed confirmed by roentgenograms, but since they were not typical, a slowly growing benign tumor or a cystic fibrous osteitis had to be considered. After construction of a dental splint the tumor was excised and found to consist of partly glossy transparent masses, and on microscopic examination it proved to be a neuroma. The healing was prompt and uneventful. This tumor, also called a perineural fibroma or schwannoma, is believed to be composed of a network of cytoplasmic cylinders sheathed with collagen. The ensheathing collagen endoneurium is laid down under the direction of the Schwann cells. The latter multiply by longitudinal amitotic division of the nuclei followed by cleavage of the cylinders, which causes the typical palisade arrangement of the cells. I have recently seen a similar tumor that occurred in the maxillary incisor region and was excised in the oral surgery clinic of Harvard Dental School (Fig. 6).

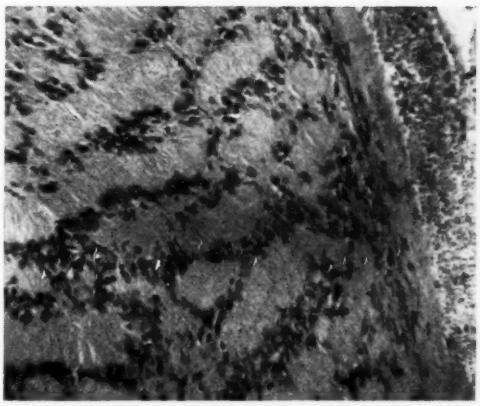

Fig. 6. Perineural fibroma from maxilla of a young woman, aged twenty.

Central angioma. This is also a very rare tumor in the jaw, which is fortunate as extraction of a tooth or trauma may result fatally. In 1934 when the literature was reviewed only 6 cases of central angioma had been reported. A dissertation on central angioma of the jaws by Kamphues (48) describes 6 cases. This author adds a new case from the University Clinic in Muenster. There was no description of the case in the review of the thesis.

Ewing's tumor. While this tumor also was considered very rare, Geschickter and Copeland (28) report 13 cases, of which 7 occurred in children and 6 in young adults under the age of thirty. The upper and lower jaws were involved with equal frequency and, in all but 3 of the cases, the symptoms, pain, and swelling were of exceedingly short duration, less than one month on the average—a very unusual finding in tumors of the jaws. The roentgen appearance is not characteristic in these cases. The treatment consisted of radical excision with cauterization, or resection and excision combined with irradiation. These tumors in Geschickter's series diminished in size rapidly, and therefore were radiosensitive, but in no case was a cure established. This is contrary to the case recorded by me earlier (Thoma, 109), which occurred in a girl aged fourteen. The tumor was microscopically verified by Geschickter and was very radioresistant. The patient died one year after resection of the jaw. However, a case (No. 294) in a girl aged nine, followed up by the Registry of Bone Sarcoma, was cured eight years after excision of the tumor combined with postoperative irradiation with radium placed within the bone cavity.

Multiple myeloma. Four cases were recorded by me (Thoma, 110), but no case has been reported since, although the jaws must be involved frequently in this disease which occurs in so many bones almost at once. The formation in bones containing red marrow favors the involvement of the mandible at the inferior border, and in the subapical area of the molar teeth, where normal remnants of red marrow may be found.

Central mixed tumors. These tumors of salivary-gland type occur from embryonic cell enclavement in the mandible, although they are not as common as peripheral tumors on the palate or in the region of the salivary glands. Rosenthal, Leipzig (1931); Malan, Turin (1932), and Thoma (1934) reported cases. Neuhaus of Cologne-Muelheim (69) reported a tumor which was removed from the mandible. Cylindromas, related to mixed tumors, also occur in the mandible and maxilla, and will be described later (Beck, 6).

Metastatic tumors. Tumors metastatic to the jaws are comparatively rare, at least only a small number of cases have been reported. This may be due, however, to the fact that metastases occur late in malignant disease when the entire skeleton is rarely roentgenographed. Therefore, metastases in the jaw are apt to be recognized only if swelling or other symptoms occur.

Carcinoma of the lip extending to the jaw through the lymphatics is quite common. Geschickter and Copeland (30) report 6 cases.

Thoma (111) recorded cases of jaw metastases with the primary lesion situated in the breast, kidney, prostate, and thyroid. A tonsillar carcinoma metastasizing to the jaw has been described by Bernard (9).

Geschickter and Copeland (30) recorded 3 cases in the Pathology Laboratory of Johns Hopkins Hospital, one an adenocystic basal-cell carcinoma originating in the mucous membrane of the nose, another a carcinoma of the prostate which invaded the lower jaw, and the third a carcinoma of the thyroid gland of a low degree of malignancy which produced a cystic area in the mandible.

Ivy and Curtis of Philadelphia (44) describe a case presenting pain and swelling of the gums in the left mandibular premolar region. Several teeth had been removed previously because of pain and loosening. Biopsy showed the soft granulomatous tissue which was curetted from the bone to be an atypical tumor. Careful examination revealed a mass high in the rectum which on biopsy showed identical tissue.

Gottlieb of New York (33) reports a metastasis of primary carcinoma in the bronchus in the anterior part of the maxilla. This became activated by extraction of a painful non-carious second incisor tooth and produced a strawberry-colored growth which extended from the extraction wound. There were also metastases to the skull, ribs, clavicle, os innominatum, and larger organs.

Treatment in these cases is palliative; irradiation is often used for this purpose.

IV. TUMORS OF THE SOFT TISSUES OF THE MOUTH

These tumors may be peripheral to the jaw formed from the periosteum and are spoken of as peripheral tumors. If formed from the gingiva they may be called epulis. An anatomical classification, however, is not practical as most oral tumors may occur in a variety of locations: the palate, the floor of the mouth, the cheeks, the lips, and the tongue. Histological classification therefore seems advisable.

Inflammatory hyperplasia. Hypertrophies of the oral mucosa or the gingiva (epulis granulomatosa) are very common and must be distinguished from true neoplasm. According to Amies (3) they are caused by parodontal sepsis, intermittent fistulas, ill-fitting dentures, suction chambers on dentures, avitaminoses, leucemias, and syphilis. They may involve, however, the formation of fibrous tissue and then are not easily differentiated from fibroma with secondary inflammatory reaction. In some instances inflammatory cells which originally infiltrated the tissue may have disappeared. Inflammatory hypertrophies are described under many names, such as epulis, papillomas, and polyps. They generally are vascular, and show a tendency toward inflammatory proliferation of the epithelium which extends in the form of retia into the underlying tissue. There is marked round-cell infiltration. They may be sessile, pedunculated, papillomatous, polypous, localized, or attached on long folds to the entire side of an edentulous jaw.

Pregnancy tumors present a special form and are associated with gingivitis gravidarum (Fig. 7). Peter of Wuerzburg (73) in a recent article agrees with the accepted view that their cause is growth stimulation due to hormonal activity associated with pregnancy. They are, as Geschickter and Copeland (31) point out, made up of granulation tissue showing areas of angiomatous proliferation and epithelial hypertrophy. Occasionally fibromas or alveolar giant-cell tumors are found which are accelerated in their growth in the first half of gestation. Two cases with a hemangiomatous histological appearance were reported by Shibata and Ohmagari (97) and Fujibayashi and Yamada (26). The first was removed six months after birth of the child, but recurred and was radically removed after eighteen months. The second patient had an epulis during each of three pregnancies. It was removed with three molars and the alveolar process on which it grew.

Peripheral giant-cell tumor. This is quite a common tumor, often called epulis or giant-cell epulis, because it occurs most commonly on the gingival covering of the alveolar bone. Amies of Melbourne (3) describes this tumor as of reddish-brown color with a purple center; it has a round smooth surface and is firm to the touch; it may be pedunculated with a broad stalk. It is painless and, if involving the interdental space, presses the teeth apart. It generally does not involve the bone. It is more common in females than in males, with an incidence of 3 to 1, and is located more often on the outer than the inner surface of the upper and lower jaw. Experimental production of this tumor was attempted by Amies in collaboration with Wright of Melbourne. They found that the injection of various doses of parathormone into the premaxilla of normal guinea pigs during pregnancy or in artificially produced occlusal strain, would not produce an epulis.

Treatment with radon gives excellent results according to Amies, but radical surgical excision with the removal of bone and contiguous teeth is generally satisfactory. The patient must be kept under observation for at least two years.

Fibroma. Clinically, soft and hard fibromas are distinguished. Amies (3) states that fibromas are

round and smooth and firm to the touch. They may be sessile or pedunculated, and are well demarcated from the surrounding tissue. They generally have a thin epithelial layer and contain collagen fibers arranged in whorls. In the soft fibroma, myxomatous degeneration is often present, the mucinous area being surrounded by a more mature type of connective tissue. In other cases the tumor shows an angiomatous character which may be of capillary or cavernous type. The latter type of tumor also appears as a soft fibroma and generally grows more rapidly than the former. Fibromas occur on the gingiva, the cheeks, the palate, and the tongue. Amies also describes a congenital type, of which 14 cases have been discussed in the literature. It involves the labial plate of the premaxilla, is pink and covered by normal epithelium, and is smooth, round, and firm, consisting of connective-tissue cells which form a fine fibrillar network. Miginiac and Escat (67) describe a voluminous fibroma of the nasopharynx which had to be removed by subtotal resection of the maxilla.

Treatment is by surgical excision including the soft tissue from which the tumor arises.

Fibrosarcoma, Amies (3) states, is comparatively rare. It forms a very irregular, ulcerating lesion in the mouth which grows rapidly. It is made up of immature connective-tissue cells with frequent mitotic nuclei. It also may form in regions covered by skin, such as the angle of the jaw. Berg (8) reports on 38 cases operated on at the University Hospital of Vienna, and Pollack (78) on 38 cases from the West German Jaw Clinic at Duesseldorf, of which 3 were inoperable and 35 were operated upon. Twenty-five of the patients lived from six months to twelve years after the operation; 4 died after operation; 3 were dismissed without improvement in their condition; and 3 lived with recurrences from two to eight years after operation; in 3 the result is unknown.

Lindemann of Duesseldorf (54) also reports a case of sarcoma which was diagnosed as epulis. The operative findings led to a general examination which revealed several metastatic tumors. This emphasizes the importance of a general examination in cases of malignancy.

Treatment must be radical. Amies recommends x-ray therapy in the very early stages; radon application through the retention of needles is not always good on account of the peculiar configuration of the growth. Pollack believes that the large number of his cures is due to radical operation and the routine use of local anesthesia. Berg could find no difference in the results in patients that received irradiation and those that did not.

Fig. 7. Pregnancy tumor and gingivitis gravidarum. Patient, aged thirty-four, five months pregnant. Tumor developed in one month to present size. Microscopic examination shows angiomatous hypertrophy of the gingiva.

Hemangioma. Darlington and Lefkowitz (19) write that since exuberant granulation tissue is an unusually common finding in the mouth, the differentiation between such lesions and hemangioma by histological evidence alone is often difficult, and many angiectatic lesions represent inflammatory neoplasms.

Bancroft, Garber, and Carr (4) report a case of bilateral hemangioma of the cervicofacial area in a white female child seven weeks old. There was a swelling of both cheeks present since birth, the left larger than the right. It extended through the entire cheek and bulged the buccal mucosa. There was a large, deeply excavated ulcer on the lower lip which caused the death of the infant at the end of eight weeks. Autopsy examination showed the tumor to be a hemangioma.

A nevus in a child fourteen months old which started to grow rapidly was reported by Lindemann (54). It proved to be due to round-cell sarcoma developing in the benign lesion.

Lymphosarcoma. A case occurring in a girl aged seven and one-half years is reported by Darlington and Lefkowitz (19). It involved the upper jaw in the region of the antrum. The child died about seven weeks after the first symptoms of the tumor occurred. Upon necropsy a diagnosis of Sternberg's disease was made.

Lipoma, leiomyoma, and rhabdomyoma. These tumors are rarely encountered. The lipoma is perhaps the most common; it is benign and often occurs as a fibrolipoma.

The rhabdomyoma, Peter (73) states, occurs as circumscribed nodes of a color somewhat lighter

than ordinary striated muscle. It is found in the lips, tongue, uvula, and jaws and is generally recognized only on microscopic examination. Twenty-one cases involving the tongue are known in the literature. The tumor may be congenital or acquired, slow-growing or malignant—rhabdomyoblastic sarcoma.

The leiomyoma is generally an encapsulated nodular tumor of benign character which may reach enormous size. Six cases involving the mouth, 1 the tongue, 1 the gingiva, and 1 the uvula have been reported in the literature, also 1 fibromyoma of the tongue, and 2 adenomyomas in the base of the tongue. Peter (73) reports a case of leiomyoma in a woman aged forty. The tumor was attached to the posterior pole of the sublingual salivary gland; it was the size of a plum and extended into the mouth and prevented the wearing of a lower denture. According to the opinion of this writer, the tumor must have taken origin from an embryonic cell rest.

Melanoma. This tumor is very rare. Darlington and Lefkowitz (19) report 3 cases in the upper jaw; 2 in white males aged sixty-three and sixty-four, and 1 in a negress aged thirty-two. In 2 cases there was so much pigment that the study and interpretation of the tumor cells were difficult. A very guarded prognosis is justifiable as local extension and metastases, as well as death from intercurrent hemorrhage and infection, are common.

Mixed tumors. Mixed tumors occur on the hard palate, and the region of the salivary glands. Central mixed tumors have been discussed (see above). Hell of Hamburg (40) reports mixed tumors of the salivary-gland type which occurred in unusual places, and comes to the conclusion therefore that they must be formed from displaced embryonic epithelium. It is generally supposed that both epithelial and cartilaginous cell rests must be present. Cartilaginous cell rests from the bronchial arches and clefts were found in the neck of a child aged six, by Boyne of Omaha, Nebraska, (11).

McFarland (64) reviewed the cases of 300 mixed tumors of which 69 had recurred and concludes that it is impossible to relate the histopathology to the prognosis. If they grow rapidly and resemble carcinoma, however, the prognosis is bad. They should not be operated upon when small, they should be allowed to "ripen." With the exception of mixed tumors of the palate, they should be allowed to reach the size of a lemon, when the probability of recurrence is greatly lessened.

Vierssen Trip of Groningen (121) studied the history of 62 patients with tumors of the salivary glands and divided them into several groups: (1) tumors of simple construction in which there is no chondroblastic and pseudomyxomatous change; these have a good prognosis even in case of recurrence; (2) tumors of composite construction in which such components are characteristic; these have a poorer prognosis; (3) cylindromas which have a questionable future; (4) benign mesenchymal tumors, fibromas and neuromas; (5) carcinomas which are mildly malignant; and (6) sarcomas which often terminate fatally.

Palatal mixed tumors of the salivary-gland type are described by Stich of Goettingen (104) with 2 original cases which were malignant. Rhoads and Mecray (83), on the other hand, state that recurrence in mixed tumor of the soft palate is extremely rare. Of 12 cases reported in the literature 3 recurred. About one-half occur in the soft palate and one-half in the hard palate. A case which recurred eleven years after operation is cited.

Cylindroma, generally classified with mixed tumors of the salivary gland, are not common according to Beck of Tuebingen (6). They occur in the parotid gland, the jaws, the scalp, the eyelids, the palate, the floor of the mouth, the tongue, the larynx, and the trachea, and, histologically, are made up of hyalin cylinders in which are found epithelial strands. Often they contain tube-like lumens with homogeneous, granular, or concentrically arranged secretion. The connective tissue of the stroma may undergo hyaline or mucoid changes. The tumors are generally smooth, and from soft to cartilaginous in consistency; they are covered with normal mucosa. Their growth is slow; they remain small if in existence as long as thirty years. Sometimes, however, they start to grow rapidly and become malignant. Two cases of malignant recurring cylindroma are cited.

Treatment by surgical excision, Rhoads and Mecray state, is comparatively easy. When the tumor is completely encapsulated dissection is not difficult and hemorrhage is slight. This accounts for the low incidence of recurrence. Too few cases have been treated with irradiation to permit any estimate of its efficacy. In mixed tumors of the salivary glands, irradiation was found to cause very little regression. The writers, however, advise postoperative irradiation (655 mgm. hours of irradiation by radium pack was used in their reported case), especially if complete extracapsular removal is not accomplished. Martin (62) reports treatment of 34 mixed tumors of the salivary-gland type of average duration of eleven years. Eighteen of these were treated, 14 by simple excision, and in 10 there was no recurrence for

from six weeks to nine years in individual cases. One patient treated by cautery excision and radon irradiation died six months later from malignant recurrence; another, after radon treatment alone, had prompt recurrence; a third is still under observation. Thirty-six patients had malignant tumors of the parotid gland with an average duration of two and seven-tenths years; 17 had surgical treatment and 6 radiotherapy; 1 had radiation after radical operation and was free from recurrence one year later. Two patients after radical surgery alone showed no recurrence for two and fifty-seven months after operation, respectively. Another patient with cautery excision is well after four years. The author concludes that radiation has not proved beneficial except as a palliative measure.

Papilloma. The opinions regarding papilloma vary; the benign lesion often cannot be differentiated from the malignant according to Hedenus of Erlangen (39). It is not proved that a benign papilloma of the mouth may become malignant, although all more recent writers take the position that all papillomas should be considered potential malignancies and removed completely by excision, or treated by irradiation, which has a marked effect on these tumors. Hedenus (39) describes a case in which several biopsy examinations showed no evidence of malignancy; radical excision was performed in spite of this result, and two pieces of the tumor showed only a benign papilloma while a third piece showed squamous-cell carcinoma.

Carcinoma. It is difficult to diagnose early lesions clinically, and the best time for effecting a cure is often lost by palliative treatment, including cauterization and incomplete excision. The dentist, writes Fitzgerald of Dubuque, Iowa (25), has occasion to examine the mouth and lips of his patients periodically. Therefore his responsibility in recognizing malignant lesions is obvious. Epidermoid carcinoma may appear on any part of the oral mucosa (Fig. 8), including the tongue and lip, but it may also occur as a primary central lesion in the jaws from epithelial cell rests—the epithelial débris of Malassez—or the lining of odontogenic cysts. In addition, Fitzgerald points out, carcinoma may form from the mucous membrane of the antrum and invade the bone to the extent that it is difficult to say whether the tumor originated in the jaw or in the antrum. Intra-osseous carcinoma is seldom diagnosed early. The first sign is expansion of the bone and spacing and loosening of the teeth. In the mandible carcinoma is apt to involve the alveolar nerve and produce neuralgic pain, followed by paresthesia. Roentgen examination may be of decided value. Surface

Fig. 8. Epidermoid carcinoma, Grade III, on buccal mucosa of a man aged twenty-nine.

lesions are generally divided into papillary, often wart-like, and ulcerating lesions.

Strout of New York (106) in a paper on tumors of the palate distinguished the following clinical forms: the ulcerating, the papillary, and the fungating type. Fitzgerald points out that in carcinoma there is a raised margin around the ulcerative area and that infiltration of the deeper structures may occur early. In some cases the surface lesion is insignificant and may be overlooked until the bone is extensively involved. Seldin (96) of New York reports such a case occurring in a man aged sixty who presented a large swelling over the right side of the face of five weeks' duration following the extraction of two loose mandibular molar teeth. There was discharge of pus and a hardened mass was visible in the region of the recent extraction. In the center of this there was a crater-like ulceration. The regional lymph glands were slightly enlarged and the patient had been treated for osteomyelitis. X-ray examination showed extensive osteolytic defects extending from the premolar region into the ramus. A diagnosis of epidermoid carcinoma was made after biopsy examination.

The importance of biopsy should be well understood, but as Fitzgerald points out, the examination should be practiced with caution. In small lesions the entire growth should be widely resected. The attention of dentists should be called to the statement that tissue attached to an extracted tooth in suspicious cases should be examined

pathologically, and no suspicious lesion should be pronounced harmless without such examination.

The treatment of oral carcinoma and results obtained are discussed in many articles. Quick (79) pleads for the close co-operative use of operative treatment by surgery and radiation, and emphasizes the fact that no matter how obviously benign a tumor of the mouth may look its removal should always be effected with utmost care and precision. For control of growth he depends on irradiation and states that there is no controversy or competition, other than that regarding the factor of quality, as to irradiation by means of radium or x-ray. The former is for application over localized areas, or more important for implantation in some form within the tissue; the latter is adapted to external application and is readily available in any quantity consistent with tolerance of the extratumoral normal tissue. Operative surgery is essential and of greatest value in many instances as an aid, but practically never to be used for the anticipated cure, *per se*, of a malignant neoplasm. Therefore it should and can be more conservative, less mutilating, and less shocking, and hence it is usually tolerated by patients who are poor risks. Surgery according to Quick resolves into three main uses: (1) for access to tumor-bearing areas, (2) for drainage, and (3) for removal of postirradiated tissues liable to gross necrosis following irradiation for growth control.

It should be remembered, says Quick, that oral cancers occur in a wide range of histological variations, and grading of the tumor is of great importance. The Grade I or fully differentiated growth is most resistant to irradiation. It may call for external therapy, implantation, and possibly some surgery. A good result obtained in this type means more in anticipation of permanence than in the more anaplastic Grades III and IV, as it is far less apt to metastasize locally or at a distance, whereas the latter which melt away rapidly under external therapy are likely to show up in almost any part or organ as spectacularly as they disappeared locally; they disseminate through both the lymphatics and the blood stream.

Méric of Bordeaux (66) advises the use of thermocauterization, or excision followed by it, to destroy the neoplasm including a wide margin of normal tissue. With this method, small lesions can be completely eradicated; in inoperable cases the results are, of course, no better than with other methods. The deep hole which is created facilitates the application of radium.

Menninger of Berlin (65) reports on the advantage of very radical surgery in cases of carcinoma of the lower jaw, which is used in the clinic of Axhausen. He advises dissection of the lymph glands of the jugular chain and excision of an increased amount of the mucosa. The resulting defect is closed with a skin flap which includes the platysma and is pushed into the wound until it appears in the mouth. Four cases operated on are free from recurrence for two, two and one-half, three, and six years, respectively.

Abel of Erlangen (1) reports that in 5 advanced cases of carcinoma of the upper jaw which recurred after treatment with surgery and postoperative irradiation, irradiation of the recurrent tumor by various methods proved unsuccessful.

Pollack of Duesseldorf (78) reports the results in 62 cases of cancer treated at the West German Jaw Clinic in Duesseldorf. These tumors occurred in the upper and lower jaws, the palate, tongue, maxillary sinus, lip, cheek, nose, and floor of the mouth. Fifty-eight were treated surgically; one was irradiated, being small; and 3 were inoperable. Of the 58 patients who received treatment, 28 lived from two months to twelve years; 6 are alive with recurrence from one-half year to seven years after operation; 3 patients died of other diseases; 3 were dismissed without benefit; 2 have not been heard of; and 1 lives with metastases. Eighteen patients died, 8 soon after the operation. The writer credits radical surgery performed under conduction anesthesia for the good results, and states that with the modern methods of plastic surgery there is no reason why radical surgery should not be used.

Marrow of New York (59), in an article abstracted in this journal (*Surg., Gynec. & Obst.*, 1937, 65: 22) states that in the New York Postgraduate Hospital the best results in cases of carcinoma of the tongue were obtained when the tongue was removed first. The next best results followed simultaneous tongue and node operation. The poorest results were obtained when the operation upon the nodes preceded that upon the tongue. Bilateral excision of the nodes gave twice as good results as excision of the nodes of the affected side only. Postoperative treatment, this writer states, was not employed in a sufficient number of cases so that any conclusions as to its value could be drawn. Among the cases treated by radium irradiation and surgery, the results of permanent eradication of the lesion were very poor.

Epstein (23) reports on the results of treatment of 314 cases of cancer of the tongue at the Onkologic Institute of Leningrad. Most patients were from forty-five to sixty years old; 149 were dismissed as incurable. The writer distinguishes three stages of carcinoma of the tongue:

Stage I. The tumor is not larger than 2 cm. and without palpable glands; 46.9 per cent of the tumors were in this group and were treated by either surgical excision with the knife or the high-frequency current, or they were destroyed by coagulation. Lately coagulation and the insertion of radium needles is favored. Of 22 patients 17, or 77.3 per cent, were well from three and one-half to eight and one-half years later.

Stage II. The tumor is larger than 2 cm. without visible infiltration of the surrounding tissue, but it has caused regional metastases, the glands being freely moveable. Forty-six and nine-tenths per cent were of this type. The glandular metastases occurred from the second to the sixth month after the first appearance of the lesion. Fifty-four per cent showed metastases in the first, second or third month, 84 per cent in the fourth, fifth, or sixth month, and almost all of the cases after the sixth month. This group is first treated with telecurietherapy, followed after from two to three weeks by coagulation and insertion of radium needles. Two and one-half weeks after the excision, block dissection of the glands is performed in both sides. Of 63 patients in this group, 16 or 25.3 per cent were well after from three and one-half to eight and one-half years.

Stage III. The tumor is large and involves the neighboring structures; there are inoperable glands on one side or operable metastases to glands on both sides. Thirty-two and eight-tenths per cent of the tumors were treated when in Stage III. Inoperable glands were given palliative irradiation and if they became moveable were excised by Crile's method. Carcinoma in the base of the tongue was treated by the insertion of radium needles with a trocar. Twelve cases of the third type were treated with no cures.

Regato of Paris (80) reports on 72 patients with epithelioma of the maxillary sinus admitted for treatment at the Foundation Curie from 1919 to 1934, and especially on 10 patients treated with roentgen therapy alone. He concludes that the radiosensitivity of these tumors is generally great, about equal to the lympho-epithelioma. Five of the 10 patients had very extensive tumors; none of these survived. Two died two or three weeks after treatment of short duration. Two others died, one six, the other eighteen months after treatment, after recurrences complicated by necrosis of the maxilla. The fifth died eighteen months after treatment which extended over about three months and was followed by gradual recurrence. Of the 5 other patients who had lesions more or less localized in the suprastructure or infrastructure of the maxilla, 4 remained cured for from five to fifteen years. One patient, after treatment and local healing, developed submaxillary adenopathy of rapid evolution and died six months after treatment. Complications caused by treatment in these cured cases were loss of vision, corneal ulcer and loss of the eye, and radio-necrosis of the skin requiring four years to heal.

Elling (22) reports the result of teleradium irradiation of buccal and jaw tumors at the clinic of Lund. He states in an article reviewed in this journal (*Surg., Gynec. & Obst.*, 1937, 65:100) that in the last ten years irradiation therapy has become the preferred method in treatment of oral carcinoma. The following difficulties are presented:

In carcinoma of the cheek an overdose may result in disintegration of the tissue. In carcinoma of the mucosa of the mandible the radiosensitive periosteum may be affected, and large doses of treatment may lead to bone necrosis, especially in the presence of infection. Among 38 cases of carcinoma of the cheek, there were 22 five-year cures. Of 41 cases involving the mandible 9 were cured. The treatment consisted of teleradium combined with roentgen therapy, electro-endothermy, surgery, and intubation with radium needles. Many of the cases were far advanced, and in other clinics would not have been accepted for treatment.

Schoenbauer (91) gives the following:

TABLE II.—COMPARISON OF SURGICAL AND IRRADIATION RESULTS IN ORAL CARCINOMA

Location	Surgical treatment			Radiotherapy		
	No. Cases	Radically treated	3 yr. survivals	No. Cases	Radically treated	3 yr. cures
Tonsils	52	26	2	83	74	11
Cheek	38	28	2	30	20	5
Gums	34	21	2	18	11	0
Mouth	30	19	3	20	17	2
Tongue	172	127	22	141	120	20
Summary	326	221 67%	31 9.5%	292	242 83%	38 13%

The keynote of the article is closer co-operation between radiotherapy and surgery.

Pack (72) gives a plan for treatment of cancer with small quantities of radium. He outlines a very workable plan to determine the quantity of radium to be delivered to any tumor. The unit of doses recommended is the threshold erythema dose used at the Memorial Hospital according to Martin and Quimby's valuable tables. The following treatment is recommended for oral tumors:

Cancer of the lip. Cells are imbedded on the inner side of a moulage to the extent of 0.5 cm. A dose varies from 0.75 to 1 m.c.hr. for every square centimeter of tissue treated.

Cancer of the tongue. Dorsolingual anterior cancer is treated by the insertion of parallel needles perpendicular to the surface and a dosage of approximately 130 m.c.hr. per cubic centimeter of tissue.

Dorsolingual posterior cancer is treated the same as the anterior type if possible. Occasionally, supplementary needles are inserted into the base of the tongue through the floor of the mouth anteriorly or through the submental or suprahyoid regions. Supplementary external irradiation is always given.

Infralingual cancer is treated with interstitial irradiation if infiltration has occurred. The dangers of interstitial irradiation in this location are emphasized. Superficial papillary carcinoma of the floor of the mouth and carcinoma of the superior and inferior alveolar processes are treated by the application of radium on a mold. Supplementary external irradiation is used.

Malignant tumor of the antrum or the superior maxilla. Surgical resection is the sole method of treatment for an osteosarcoma or a chondrosarcoma of the antrum or the superior maxilla. Radium irradiation of the epidermoid carcinoma is preceded by surgical drainage and épuchage. An incision is made along the nasolabial fold and through the upper lip to permit correct placement of the tubes or needles. Roentgen irradiation is employed as a pre-operative and supplementary measure. In advanced cases radical excision is done.

Metastatic carcinoma in the cervical lymph nodes. The great problem in the management of these nodes is the consideration of the indications and contra-indications for a radical or partial cervical dissection and of when to employ radiation therapy in lieu of surgical excision. Pack believes that James J. Duffy has furnished the best answer:

INDICATIONS*	CONTRA-INDICATIONS*
1. Metastases limited to one node or group of nodes.	1. No apparent metastatic involvement of nodes.
2. No perforation of capsule of lymph nodes.	2. Perforation of capsule by carcinoma.
3. Primary lesion controlled or controllable.	3. Primary lesion uncontrolled or uncontrollable.
4. Opposite side of neck free from disease.	4. Crossed or bilateral metastasis present.
5. Primary lesion limited to one side of oral cavity.	5. Extension of primary lesion to or beyond the midline.
6. Primary lesion composed of highly differentiated cells.	6. Primary lesion composed of highly undifferentiated cells.
7. No distant metastases.	7. Distant metastases.
8. Patient in good general health.	8. Patient in poor general health or aged.
*All of these indications must be present for dissection.	*Any one of these contra-indications precludes radical dissection.

A table giving the five-year cures in oral carcinoma in the Johns Hopkins Hospital at Baltimore was published by Geschickter (27):

TABLE III.—FIVE-YEAR CURES IN ORAL CARCINOMA

	No. of cases	Per cent of cures	Per cent of cures by location
Lip	395	52	
Upper			85
Lower			49
Tongue	223	15	
Tip			20
Midborder			11
Under surface			11
Base			5
Mucous membrane	213	17	
Lower gingiva			25
Floor of mouth			20
Cheek			10
Palate			10

Martin of New York (60) writes that intra-oral carcinomas are generally not very sensitive to irradiation and therefore both external and interstitial exposure are indicated for their control. The external irradiation is used first and followed immediately by implantation of a small or moderate dose of radon seeds. Adequate dosage is often accompanied by certain untoward effects, which can be prevented by use of the open mouth as a portal of entry for the insertion of a metal cylinder attached to the tube holder. In another article Martin (61) gives the five-year end-results in the treatment of cancer of the tongue, lip, and cheek at the Memorial Hospital in New York. Successful results in the determinate group (after elimination of patients not followed up or dead as a result of other diseases) were as follows:

TABLE IV.—SUCCESSFUL RESULTS IN CANCER OF TONGUE, LIP, AND CHEEK

Location	No.	Five-year end-result No.	Five-year end-result Per cent
Cancer of tongue	290	74	26
Cancer of lip	188	130	69
Cancer of cheek	91	28	30

Factors influencing the prognosis are important. The wide difference in clinical material makes it difficult to evaluate properly the comparative merits of contemporary treatment methods in cancer. Martin suggests a form for the reporting of net percentages of five-year end-results. The following table shows factors influencing the prognosis in 322 cases of cancer of the tongue observed at the Memorial Hospital from 1927 to 1931.

TABLE V.—FACTORS INFLUENCING THE PROGNOSIS OF CANCER OF THE TONGUE

	Total number of cases	Number of five-year cures	Per cent of five-year cures
Age in years			
Below 40	23	9	39
41 to 50	48	10	33
51 to 60	120	26	21
Over 60	131	23	16
Sex			
Males	276	48	18
Females	46	16	35
Stage of disease			
"Operable"	90	50	55
"Borderline"	42	18	42
"Inoperable"	190	10	5
Position of growth			
Anterior third	47	13	27
Middle third	180	53	20
Posterior third	95	8	8
Metastases			
None at any time	125	51	40
Present on admission	113	6	5
Developed after admission	84	19	22
Histopathology			
Epidermoid carcinoma			
Grade I	51	23	45
Grade II	177	35	25
Grade III	23	1	4
Lympho-epithelioma	2	0	0
Transitional-cell carcinoma	14	2	14
Adenocarcinoma	5	0	0
Not Classified*	50	13	26
Associated leucoplakia	69	26	37
Associated syphilis	70	14	20

*Biopsy positive but unsatisfactory for exact classification.

The use of surgical prostheses is also of interest in tumor surgery. Roy (88) of Montreal points out the advantage of a vulcanite prosthesis when an operation on the palate leaves a perforation, or for perforations caused by irradiation therapy. Such appliances must be perfectly adapted and, if teeth are present, fastened by means of clasps. The purpose is to prevent regurgitation of food and voice disturbance.

Reichenbach of Leipzig (81) describes prosthetic appliances for many purposes: (1) splints constructed to prevent fracture and to hold remaining parts of the bones in position; (2) prostheses either to be inserted immediately or constructed later. These also serve to prevent malposition of the remaining parts of the jaw, as well as contraction of the soft tissue. In cases of resection of half, or the posterior part, of the mandible in which no future osteoblastic operation is planned, Reichenbach advises that no attempt be made to construct an artificial joint, but instead that an intermaxillary hinge attached to dentures be used which may also serve as obturator. If the jaw is to be repaired by a bone graft later, these appliances are not satisfactory, because the pocket in which the appliance rests may subject the newly formed epithelium to irritation, and infection may thus set in. Simple splints are more useful in such cases, and with the use of a guide plane or elastics, it is still possible to hold the remaining part of the jaw in position. Obturators are described for use after resection of the maxilla to close perforations of the hard palate or obliterate defects of the soft palate. An appliance useful to prevent union between the soft palate and the posterior wall of the pharynx is pictured and described.

Preparation of the mouth and teeth before the beginning of any course of curative treatment is emphasized by Lund of Boston (55). In most cases this will entail extensive extraction of teeth, rather than cleaning and filling. It is very important, and a week or ten days may be spent for extraction and partial healing of the sockets before operation or radiation. The procedure will serve to save many serious post-treatment infections.

Sarasin of Geneva, Switzerland, (90) also stresses proper dental care in the treatment of cancer. He recommends extraction of all carious, abscessed, and pyorrhetic teeth and roots, stating that neglect of this procedure may later lead to irradiation necrosis of the jaw. He also points out that the dentist should be advised about patients who have had irradiation and warned to proceed carefully with any dental operations. The extraction of teeth even after several years may lead to stubborn infection and even complete sequestration of the jaw. The calcium salts in the bone retain radium and cause secondary irradiation of the surrounding tissue.

Protection of the surrounding organs and uninvolved tissue is of great importance in irradiation treatment. Ackerman (2) describes the construction of protective shields which limit the effects of irradiation to the area occupied by the cancer. These shields are designed to prevent irradiation of the involved maxillary bones, the lips, tongue, palate, cheeks, floor of the mouth, and salivary glands. The construction requires a knowledge of

prosthetic dentistry. A lead shield 1/8 in. in thickness, cut and shaped to fit over the area to be protected is vulcanized into rubber in the form of a denture that exactly fits over the teeth, and is worn during the treatments. Many ingenious types of shields are illustrated in this article, with detailed description of their construction.

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ABSTRACTS OF CURRENT LITERATURE

SURGERY OF THE HEAD AND NECK

HEAD

Mela, B.: The Pathogenesis and Treatment of the Ankyloses of the Temporomandibular Joint (Patogenesi e terapia delle anchilosi dell'articolazione temporo-mandibolare). *Minerva med.*, 1938, 29: 553.

All disturbances of the temporomandibular joint are unusual. Ankylosis usually results from an acute arthritis, rarely from the chronic condition. Among the causes of the arthritis are trauma, gonorrhea, extension from nearby infections, and metastasis from generalized acute infection. Trauma is a fairly common cause of trouble especially when the cartilages are injured or when infection and suppuration supervene. Gonorrhea in the newborn is often associated with the specific conjunctivitis and may be unnoticed because all attention is concentrated on the eyes. Gonorrhea is more uncommon as the cause of ankylosis in adults, but it may produce a very acute and painful arthritis. There also are atypical cases without an acute onset in which a deforming arthritis may appear. Osteomyelitis of the ascending ramus of the mandible may develop by extension from an otitis media, suppurative parotitis, or suppuration of the pre-auricular lymph nodes. Metastatic arthritis in the course of generalized infections occurs especially in scarlet fever and typhoid fever.

In general, all these forms of acute arthritis are treated with warm packs, vaccines, or intravenous antiseptic solutions. If there is pus in the joint arthrotomy may be done. Mild inflammations may leave the joint undamaged, but when the articular cartilage is damaged ankylosis is almost an inevitable result.

Dufourmentel records the following incidence of the factors leading to ankylosis: trauma in 27 per cent, otitis in 11, gonorrhea in 9, scarlet fever in 8, typhoid fever in 1.8, and diphtheria in 4. Unknown or possibly congenital factors are present in 13 per cent of the cases.

Age incidence indicates a preponderant frequency in children.

The degree of ankylosis may be partial or complete. X-ray examination indicates whether there is an actual bony bridging of the joint with true bone. In youth the presence of ankylosis results in a growth disturbance of the mandible. In the presence of unilateral ankylosis only the corresponding half of the mandible is deformed. Bilateral ankylosis results in the characteristic "Vogelgesicht," in which the mandible seems to be absent.

The treatment in general is based upon an operative arthroplasty, often with resection of the head of the mandible. Movement must begin soon after the operation. Various devices are described which may assist in the postoperative movements of the jaw.

A. Louis Rosi, M.D.

EAR

Jerlang, E.: Otogenous Non-Purulent Encephalitis. *J. Laryngol. & Otol.*, 1938, 53: 283.

Jerlang directs attention to uncomplicated otogenous non-purulent encephalitis, and states that in 1921 Borries was the first to describe this picture as an independent clinical entity. Reliable clinical observations have been published by several authors. In cases involving the cerebrum the symptoms subsided very slowly, and the patients were discharged after a period of from one to four months. According to the literature, otogenous non-purulent encephalitis occurs infrequently, possibly because of the difficulty in the establishment of a diagnosis and also because the entity is frequently called pseudo-abscess.

The author reviews one of his own cases. He states that the morbid condition, developing either quite suddenly or quite slowly, occurs most often among children and young adults in association with both acute and chronic ear suppuration. In the absence of abscess formation, the diagnosis of otogenous encephalitis is extremely difficult. In those cases in which it is assumed that the pathological processes lie in the silent areas of the brain, or are limited in extent, the symptoms are so vague and atypical that the affection is either unrecognized or misinterpreted. In pronounced cases the symptoms are comparable to those presented by a cerebral abscess, "abscess symptoms without abscess." As a rule the diagnosis will be made by exclusion.

In otogenous non-purulent encephalitis the temperature is usually, but not always, high. The pulse rate is proportionate to the temperature. The cerebrospinal fluid hardly affords any diagnostic assistance, since the cellular findings and the pressure are inconstant factors. Jerlang believes that the knowledge of otogenous encephalitis as an autonomous affection can be of importance in the estimation of the prognosis of apparent or suspected cerebral abscess, particularly in those cases in which the puncture of the brain fails to reveal pus. Such cases should not be considered hopeless and, consequently, tempt the surgeon to incise the brain without restraint under the assumption that the patient's only chance for recovery is the evacuation of pus. On the whole, the prognosis of otogenous encephalitis can be considered favorable.

Noah D. Fabricant, M.D.

NECK

McEwan, P.: Clinical Problems of Thyrotoxicosis. *Brit. M. J.*, 1938, 1: 1037.

Although the surgical treatment of thyrotoxicosis has been improved considerably, a steady increase in the deaths from this condition is being observed. McEwan has analyzed all deaths from this cause which occurred in England and Wales during the year of 1936.

The geographical distribution shows a remarkable parallelism to similar surveys made during the period from 1913 to 1919, and this distribution, rather than the stress of modern living, apparently accounts for the incidence of simple goiter.

The author's survey shows that an unusually high proportion of the patients were between ten and thirty years of age, and that the ratio of the mortality in men to that in women is one to eight or nine.

There were 276 deaths following operations. Chest complications and deaths following anesthesia appeared to be disproportionately high.

There were 1,420 medical deaths. Nine hundred and eight patients died of cardiac complications and 298 of these had auricular fibrillation. Vascular complications, hemorrhage, thrombosis, and embolism occurred in 91 and nephritis occurred in 21. The remaining complications were varied. Two hundred and nineteen deaths were due to uncomplicated thyrotoxicosis. Some authors believe that iodine has caused an increase in medical deaths and that it should be used pre-operatively only.

It is probable that many deaths occur because of delayed diagnoses, since thyrotoxicosis may wear various masks, such as cardiac, mental, abdominal, and general debility, and there may be an absence of detectable goiter.

Surgeons are wary of the question as to whether the death rate can be reduced by surgery.

In the author's own material, comprising 190 cases, 67 per cent of the patients were fit for work after operation, while 33 per cent were only partially benefited or were not benefited because of associated diseases.

FRED S. MODERN, M.D.

Perkin, H. J., and Lahey, F. H.: Exophthalmic Goiter: Relation Between the Blood Iodine Level and the Duration of Symptoms in 305 Cases. *Arch. Int. Med.*, 1938, 61: 875.

The blood iodine level is above normal in about 70 per cent of all cases of hyperthyroidism. In cases in which the iodine level is normal, the therapeutic response is less prompt than in cases in which the blood iodine level is high. Response is more prompt also in recent cases than in those in which symptoms are of long standing. The question of the possible correlation between the blood iodine level and the duration of symptoms arose as follows:

Three hundred and five patients (267 women and 38 men) were studied with this purpose in mind. One hundred and sixty-three cases were of nine months' duration, or less. The iodine content was elevated in 86 per cent and was normal in 14 per cent. One-half of the cases of from nine to eleven months' duration had elevated iodine values, but of the cases lasting a year or longer, 36 per cent had elevated values and 64 per cent were normal. The average basal metabolic rate was about the same in all time groups.

Hyperplastic thyroid tissue tends to be low in iodine. The longer the disease lasts, the more depleted become the iodine stores of the body. It is easy to explain how an increased thyroxin secretion can cause the symptoms of hyperthyroidism in cases of short duration, in which the blood iodine is elevated, and how such cases would respond favorably to subtotal thyroidectomy. Further explanation is necessary, however, in cases in which the blood and thyroid gland are deficient in iodine, as such cases cannot be attributed solely to the hypersecretion of an iodine-containing product of the thyroid gland.

FRED S. MODERN, M.D.

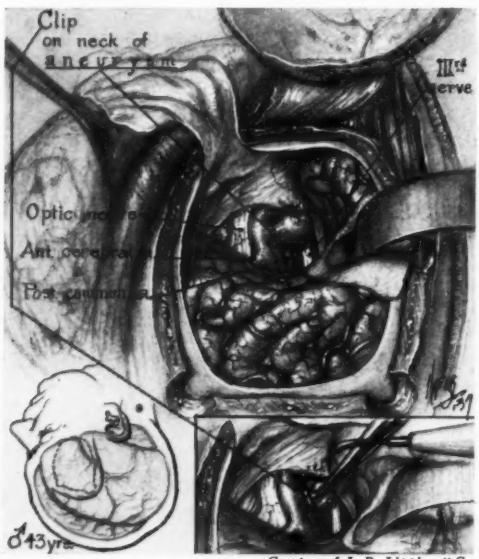
SURGERY OF THE NERVOUS SYSTEM

BRAIN AND ITS COVERINGS; CRANIAL NERVES

Dandy, W. E.: Intracranial Aneurysm of the Internal Carotid Artery. *Ann. Surg.*, 1938, 107: 654.

Aneurysms of the circle of Willis are not uncommon. They are the cause of most subarachnoid hemorrhages. The majority of these aneurysms do not show any localizing signs. Those in which there is paralysis of the third nerve, which condition was found to be present in the author's case, are exceptional. According to Sands, 47 per cent of aneurysms along the posterior communicating artery produce signs which are referable to the third nerve.

The indications for operation on aneurysms at the circle of Willis which cause only subarachnoid hemorrhage are not clear. Without knowledge as to the side of the circle of Willis upon which the aneurysm is located, operation is not justified. When a patient has had a subarachnoid hemorrhage and has recovered, operation is not indicated because hemorrhage may not recur for a number of years, although this is not the usual course. During a subarachnoid hemorrhage, and immediately after a hemorrhage has subsided, one would not dare to operate, as the intracranial space needed for operation would be occupied by blood. For cases with palsy of the third nerve, the indications are clear. If subarachnoid hemorrhages recur and the prognosis seems hopeless, operation is perhaps indicated if there is a suggestion as to the side upon which the aneurysm is located. Arteriography may be of considerable aid in such cases.



Courtesy of J. B. Lippincott Co.

Fig. 1. Drawing of aneurysm. Inset on the left shows the operative approach with the author's concealed incision. Inset on the right shows clip placed on the neck of the aneurysm and the cautery shrivelling the sac.

Dandy reports a case of aneurysm of the circle of Willis which he believes to be the first one in which an attempt at cure was made by a direct attack on the aneurysm. It was that of a forty-three-year-old male alcoholic patient who, in the course of about forty-eight hours, lost the function of his right third nerve. At operation an aneurysm with a narrow neck springing from the internal carotid artery, was found (Fig. 1). An ordinary flat silver clip was placed over the neck of the sac and tightly compressed, which obliterated it completely. The sac, distal to the silver clip, was then thrombosed with the electrocautery. DAVID J. IMPASTATO, M.D.

Matas, R.: Aneurysms of the Circle of Willis. *Ann. Surg.*, 1938, 107: 660.

There are 3 classes of arterial aneurysms in the brain:

1. The miliary aneurysms of the central arteries. These are the most frequent and most fatal, and are beyond surgical reach except when they create circumscribed hematomas in the substance of the brain.

2. The larger aneurysms of the carotid tracts up to the circle of Willis. This type may be treated by extracranial ligation of the internal and common carotid trunks in the neck.

3. An intermediary group arising from the circle and its surface branches. These are not controllable by extracranial ligation of the parent trunks in the neck, but can be treated by a direct intracranial attack. Operation in these cases should be preceded by accurate localization of the aneurysm by the usual methods, supplemented by cerebral angiography, which is the only procedure which will show definitely that the pathological lesion is an aneurysm and nothing else.

The effect that the removal of an aneurysm may have on the area supplied by the obliterated vessel, through ischemic suppression of its blood supply, should be seriously considered. It is well to remember that it is practically impossible to obliterate the vast majority of these aneurysms without interruption of the circulation in the circle and serious impairment of the nutrition of the area of the brain that is supplied by the arteries given off from the circle, beyond the obliterated branch. It is also possible that in extirpation of an aneurysm in the circle, the obliteration may be indefinitely extended along the circle by progressive intravascular thrombosis. DAVID J. IMPASTATO, M.D.

SYMPATHETIC NERVES

Allen, E. V., and Adson, A. W.: The Physiological Effects of Extensive Sympathectomy for Essential Hypertension: Further Observations. *Ann. Int. Med.*, 1938, 2: 2151.

Extensive sympathectomy can be carried out safely in patients suffering from essential hypertension. In 311 operations on 156 patients at the Mayo Clinic there were no operative deaths. The operation does not disable and it produces only minor effects on the sexual function, sweating, and the intestines. Only an inconsequential effect on the blood pressure was produced in 20 per cent of the 124 patients from whom information relative to their blood pressure and general health following postoperative dismissal from the hospital was secured. In 28 per cent of these, the reduction in the blood pressure was only temporary; in another 28 per cent there was significant reduction of blood pressure, which, however, did not approach normal levels; and in 24 per cent the blood pressure was greatly reduced when compared with the pre-operative reading.

Headache, nervousness, and pain in the left side of the thorax are relieved in a large percentage of instances, regardless of whether the effects of operation on the blood pressure are poor or good. Dyspnea and fatigue on exertion occur commonly after operation, but tend to disappear gradually.

No infallible method for selecting patients for operation is available. However, when the diastolic blood pressure decreases to less than 110 as a result of rest, administration of amytal, and the injection of pentothal, and when sclerosis of the retinal arteries is absent or slight, the patient will probably get a good result from operation. On the other hand, when there is advanced sclerosis of the retinal arteries, when the maximal diastolic blood pressure exceeds 150, and when the diastolic pressure does not decrease to less than 120 as a result of rest, the intravenous injection of pentothal sodium, or the administration of sodium amytal, the probabilities that the patient will receive good results from operation are slight.

Allen and Adson conclude that it is advisable to operate on more patients who have mild hypertension and on fewer patients who have severe hypertension.

Koch, C. F., and DeSavitsch, E.: The Treatment of Disseminated Sclerosis by Sympathectomy and Ganglionectomy. *Brit. M. J.*, 1938, 1: 1254.

The authors discuss the theoretical aspects of the cause of disseminated sclerosis. They agree with the work of others indicating that this lesion is probably produced by simple mechanical interference with the blood supply. When the pathological changes in disseminating sclerosis can be attributed to an ischemic phenomenon resulting from a spasm of the blood vessels supplying the parenchyma of the brain or spinal cord, treatment should be directed toward decreasing the alleged vascular constriction, which will permit a better blood supply to the involved area.

The authors report their experiences, based on 26 operations performed on 15 patients with advanced disseminated sclerosis, in whom the upper thoracic and lumbar sympathetic ganglion and trunks were extirpated. The pre-operative care and the technique of the operative procedures are described in detail. The approach is through a semilunar incision, made just above the clavicle and extending from the border of the trapezius muscle to approximately 1 cm. beyond the midline. The vertebral artery is stripped of its sympathetic plexus over an area of from 1 to 2 cm. The stellate ganglion and the vertebral nerve are removed. There were 2 deaths following this operation. One was from embolus and the other from hemorrhage of the thyreocervical trunk. A Horner's syndrome was observed in every case. The patients avoided extreme exertion for several months after operation. There was a transit incontinence in about one-third of the cases. Ten of the 14 patients were observed for from six to fourteen months after operation. Practically every one responded favorably and the authors are convinced that this treatment in advanced multiple sclerosis should be given further trial.

ROBERT ZOLLINGER, M.D.

SURGERY OF THE THORAX

CHEST WALL AND BREAST

Romano, S. A., and McFetridge, E. M.: The Limitations and Dangers of Mammography with Contrast Mediums. *J. Am. M. Ass.*, 1938, 110: 1905.

Reports in the literature of the value of mammography and of the harmlessness of stabilized colloidal thorium dioxide under these circumstances led the authors to undertake its use in a personal investigation. The material included 25 patients, 23 of whom were operated upon later. In 13 of these 23 patients the mammographic diagnosis agreed with the clinical diagnosis and was later confirmed in the laboratory. In the other cases the diagnosis was either not definite or was actually incorrect. The most serious errors occurred in cases of malignant disease. These errors were found to be evident clinically but were not revealed by mammography.

In 4 of the 25 patients the injection of iodized oil or of colloidal thorium dioxide gave rise to foreign-body reaction, and the condition of 3 patients became very severe. In 2 of these amputation of the breast would have been necessary because of the reaction even if it had not already been planned for the original condition.

An experimental study on animals resulted in foreign-body reactions in more than 50 per cent of the cases, all reactions being similar to those noted in the clinical cases. The various agents used experimentally, all of which were satisfactory from the radiological standpoint, were sometimes followed by reactions. Lavage of the breast after injection did not prevent the reaction in all cases, nor did physiological lavage, brought about by the act of nursing, prevent it.

These authors do not feel that the method, as it is now employed, contributes diagnostic aid of sufficient value to warrant the risks of the serious reaction that may follow it. Until an agent is discovered which is non-irritating to the breast tissues and which is at the same time satisfactory from the radiological aspect, they do not advise the use of mammography by means of contrast mediums.

J. Daniel Willems, M.D.

Frantz, V. K.: The Prognostic Significance of Intracellular Mucicarminophilic Material in Carcinoma of the Female Breast. *Am. J. Cancer*, 1938, 33: 167.

This is a report of 130 cases of carcinoma of the breast, in all of which a radical mastectomy was done during the period from 1928 to 1932. The author reports upon the presence or absence of metastases in the axilla, the grade of the tumor according to the plan of Haagensen, and the presence or absence of mucicarminophilic material in the stained sections.

The follow-up study was conducted upon 97.1 per cent of the cases for a period of from five to nine years. It was found that the mucicarminophilic material appears in all grades of the tumor, but the relative amounts found had no significance. It appeared that the presence or absence of this material in the cells of carcinoma of the breast was related to the length of life after operation; the presence of intracellular mucicarminophilic material was a favorable sign and of aid in the prognosis of the Grade II tumors.

The author points out that no histological characteristic has yet been found which carries the weight of the well known clinical findings, such as age of the patient, extent of the local tumor, and the presence of axillary metastases.

J. Daniel Willems, M.D.

Stout, A. P.: The Relationship of Malignant Amelanotic Melanoma (Nevocarcinoma) to Extramammary Paget's Disease. *Am. J. Cancer*, 1938, 33: 196.

The author reports a case of a tumor of twelve years' duration occurring in a woman seventy-one years old. He believed the tumor to be a pigment-free malignant melanoma, the primary manifestations of which were indistinguishable from Paget's disease. This tumor appeared in the left popliteal region and consisted of a crusting lesion which occasionally bled. Eight years after its appearance it was treated by irradiation and disappeared except for one small crusting area. Four years later two small lesions were present in the original site and in addition a firm node in the left femoral region was found. These were all excised, the denuded areas covered with skin grafts, and irradiation was administered. After nineteen months death came from pulmonary metastases.

The histopathological study of the popliteal lesions showed the epidermal layer to be intact; the rete pegs thickened and elongated to three times their normal size. The tumor cells were rounded or elongated with hyperchromatic nuclei, clearly defined nuclear markings, and only one nucleolus. Mitoses averaged one in every five high-power fields. The cytoplasm was granular and neutrophilic, and the cell membrane distinct. The Fontana stain showed no trace of melanin. Similar study of the femoral lymph node showed practically complete replacement of the lymphoid tissue by tumor cells. These were arranged in thick cords separated by slender collagen bands near the capsule, and by thick fibrous strands near the center. The cells were large, rounded, and with large hyperchromatic nuclei placed centrally. Mitoses averaged one in each high-power field. No trace of pigmentation was apparent, either grossly or with the Fontana stain.

Such a lesion could be one of only two conditions: (1) extramammary Paget's disease or (2) intra-epidermal melanoma without pigment formation. The chief factor which enables the author to differentiate between the two was the primary site. Every unquestioned case of extramammary Paget's disease has occurred in the male or female genital regions, or in the axilla where there are apocrine glands. The morphology of the metastases further pointed to the diagnosis of melanoma rather than Paget's disease. J. DANIEL WILLEMS, M.D.

TRACHEA, LUNGS, AND PLEURA

Culp, O. S.: Primary Carcinoma of the Trachea. *J. Thoracic Surg.*, 1938, 7: 471.

Only 433 primary tumors of the trachea have been reported up to 1937, and 147, or 34 per cent, were carcinomas. The carcinomas occurred most frequently near the bifurcation of the trachea, more frequently in the upper third and least frequently in the middle third. The tumor was usually located in the posterior wall of the trachea and in only 5 cases was there an annular lesion.

There is no correlation between the incidence of metastases and the age periods. The squamous-cell variety had most often metastasized. The metastases were usually regional, involving the esophagus, and the mediastinal, peribronchial, and cervical glands.

The age of the patients varied from eighteen years to eighty-two years, and there was a fairly equal distribution of the condition between thirty and seventy years of age. Sixty-three per cent of the patients were males.

In general, the carcinomas fall into two main groups, (1) those arising from glandular epithelium and (2) those arising from surface epithelium. The predominant cell in the latter group may be columnar, cylindrical, basal, or squamous. Of these the squamous-cell carcinoma is the most common.

The author adds 2 new cases of primary carcinoma of the trachea to the literature. One patient was a sixty-eight-year-old man who died of a metaplastic squamous-cell carcinoma of the trachea with direct invasion of the mediastinum, regional lymph nodes, and metastases to the esophagus. The second patient was a fifty-four-year-old woman who had a metaplastic transitional-cell carcinoma of the trachea with direct invasion of the mediastinum and the thyroid gland.

From the cases previously reported and the 2 cases presented it is found that most patients die within one year, but a few isolated patients lived as long as one year. The type of therapy had little, if any, effect on the outcome. EARL O. LATIMER, M.D.

Holst, J.: The Symptoms and Treatment of Bronchiectasis (Klinik und Therapie der Bronchiektasiekrankheit). *Finska läk.-sällsk. handl.*, 1937, 80: 794.

The use of bronchography and bronchoscopy in the diagnosis of pulmonary conditions has resulted in earlier recognition of bronchiectasis and more radical treatment of that condition. The author discusses only the so-called primary bronchiectasis. A number of these cases are undoubtedly congenital; others occur in youth following influenzal pneumonia or diphtheria. Of more importance to the surgeon is the site of the disease. Clinical symptoms usually follow only after infection. The usual clinical picture in bronchiectasis is the result of a vicious circle, the combined action of retention and infection, and this condition can be interrupted only by attack of the retention.

Most of the patients with bronchiectasis died of a pumonary complication; according to Blake 34 per cent died of bronchopneumonia and 16 per cent of metastatic brain abscess. The author reports 19 cases of primary bronchiectasis, in which 9 of the patients were under ten years of age and 7 were over twenty years of age. Among the important symptoms mentioned, drumstick fingers were present in 8 patients. The clinical diagnosis is made by means of x-rays and bronchography. In the differential diagnosis tuberculosis is most important; 9 of the 19 patients whose cases were reported had been inmates of tuberculosis sanatoria up to six years. Pulmonary abscess is also confused with bronchiectasis occasionally. Other conditions may be excluded by bronchoscopy.

From the literature it is clear that the radical treatment must be lobectomy. Collapse therapy, consisting of pneumothorax, phrenicotomy, and thoracoplastic operations, offered nothing. Lobectomy was performed 10 times. One patient on whom a bilateral lobectomy was performed died of empyema. The 8 other patients on whom lobectomy was performed recovered. One of these is still under treatment, the 7 others are well. The operative technique employed was that of Brunn, an American surgeon. The attempt to dry up the bronchi by means of the bronchoscope and suction was not encouraging. Deep anesthesia with a mixture of ether, oxygen, and carbon dioxide was used; it was preceded by large doses of morphine and scopolamine. An absolute contra-indication to the operation is the absence of two normal lobes of the lungs.

(GERLACH). LEO A. JUHNKE, M.D.

Sauerbruch, F.: The Status and a Critical Study of the Operative Treatment of Bronchiectases and Pulmonary Tuberculosis (Stand und Kritik der operativen Behandlung der Bronchiektasen und Lungentuberkulose). *62 Tag. d. deutsch. Ges. f. Chir.*, Berlin, 1938.

The author's report is based on statistics from more than 500 clinics, hospitals, and sanitoria in Germany and elsewhere. Among the surgically important forms of bronchiectasis, the traumatic, the contraction bronchiectasis, and finally, the congenital dilatation resulting from malformations of the bronchial branches are discussed in detail.

The unilateral lobectomy of the Munich Clinic had to be abandoned because of retraction of the

bronchus stump into the mediastinum. As a result, a procedure of two or more stages was developed, as described by Sauerbruch at the 1934 German Surgical Congress. Brunn has revived the one-stage lobectomy, but he uses a different technique. An important advance is drainage of the chest cavity. One-stage lobectomy is indicated chiefly in younger individuals with localized findings. The two-stage procedure is safer and easier on the patient. An in-between method is that of Nissen. Packing and drainage are included in the armamentarium of surgical therapeutic methods.

The surgical treatment of pulmonary tuberculosis must depend on the character and development of the disease. The important factor consists of choosing the proper time. Some of the newer recommendations ignore the old principles. Historical consideration reveals that the conceptions of Quincke, Spengler, and Forlanini-Murphy form the entire basis for the modern treatment of pulmonary tuberculosis; all of them seek the same goal, relaxation, narrowing, and compression of the lung. In the first phase of surgical treatment, the ground-work was laid: paravertebral resection from the first to the tenth or eleventh rib, apicolysis, anterior plastics, partial plastics over the upper lobe, phrenicotomy, and packing. Further development urged early operation, often for external reasons. Their conditional justification is critically discussed, in relation to the character of the disease. The proponents of general early operation overlook the frequency of spontaneous healing of cavities.

Extrapleural pneumothorax and oleothorax cannot yet be generally recommended, because of their dangers. Their evolution, however, is desirable, as is also the substitution of a better medium for paraffin in plombage. The method has proved of value in the hands of many surgeons, when used with proper indications and technique. Good results are obtained in combination with other methods, in bilateral tuberculosis. A further advance consists in the abandonment of routine phrenicotomy. The present use of thoracoplastic procedures is gratifying. It is agreed that so-called apical plastic surgery should be considered in only very circumscribed lesions. More extensive partial plastic surgery is merely a gradation of the old paravertebral rib resection. This has retained its old limit of indications. With circumscribed findings (apical and upper lobe cavities), the resection of 7 or 8 ribs with dropping of the shoulder blade is generally recommended. Recently, the swing has been away from this in favor of mobilization of the upper anterior chest wall (the old anterior plastic).

In his concluding remarks, the author mentions certain dangers: the alienation of the practicing surgeon, increasing exclusion of the University Clinics and Hospitals from active co-operation on the question of the surgical treatment of pulmonary tuberculosis. The final solution of these problems remains with the personality of the physician.

(Sauerbruch). Leo M. Zimmerman, M.D.

ESOPHAGUS AND MEDIASTINUM

Henschen, C.: The Operative Treatment of Rupture of the Varices of the Esophagus by Subdiaphragmatic Occlusion of the Veins (Die operative Behandlung der Varicenruptur der Speiseroehre durch subdiaphragmatische Venensperre). *62 Tag. d. deutsch. Ges. f. Chir.*, Berlin, 1938.

Massive hemorrhages from ruptured varices of the esophagus almost always run a fatal course. "Internal" methods of hemostasis, hemostatic transfusion, tamponade of the esophagus, and ligation of the large arterial stems in the neck are useless. Efforts at surgical aid are, therefore, directed toward the idea of stopping the source of hemorrhage at the site of the bleeding itself, i.e., toward carrying out local hemostasis.

Hemorrhages from the venous areas of the esophagus arise from different anatomicoconditional regions: (1) (rarely) from an "angioma venosum" of the esophagus; (2) (rarely) from congenital phlebectasias or vascular anomalies; (3) (rarely) from venoparalytic "neurovarices," i.e., dilatations of veins as a result of diseases of associated regions of the nervous system; (4) from phlebitic diseases of the esophageal veins, for example, phlebitis following chronic appendicitis with death from hemorrhage and typhoid phlebitis; (5) from traumatic lesions of the esophageal veins; and (6) (most often) from static varices (compensatory venectasias) in association with previous diseases in the region of the liver (cirrhosis, syphilis) or the portal vein (thrombotic or thrombophlebitic obliteration of the vein, with portal-vein compensation by aneurysm of the hepatic artery or tumor). These compensatory dilatations of the veins, sometimes of the thickness of a lead pencil, and known in the stricter sense as "varices of the esophagus," are situated in the region of one of the accessory exits of the portal vein; they are the inferior esophageal veins draining the region of the portal vein via the vena coronaria ventriculi to the azygos vein, in the lower fifth of the esophagus or around the cardia.

The diagnosis of these particular causes of hemorrhage is based upon the clinical general findings (diseases of the liver, appendix, spleen, portal vein); upon the "typical" roentgen findings to the practiced eye, to be observed by a special technique (deformity of the cardia and of the gastric fornix, circumscribed filling defects on the posterior wall of the esophagus, circular lighter areas, a niche at the site of the rupture, a peculiar "fielding" of the esophageal relief [string-of-pearls symptom], and delayed passage of the test meal); and, finally, upon the direct esophagoscopic evidence of the varices and, in every case, of the site of bleeding or rupture.

With the aid of an operative observation it is shown that it is possible to master this so fatal hemorrhage surgically by means of a systematically planned intra-abdominal ligature occlusion of all the venous straits (vena coronaria ventriculi) leading from the infracardial zone of the esophagus by way

of a high laparotomy running parallel with the left costal border. This operation may be extended to a laparothoracotomy by a splitting of the cartilaginous costal arch and the diaphragm when ligation of the vena azygos seems to be necessary and urgent.

The toilet and clarification of the surgical pathology of the epigastric region (liver, spleen, stomach, and cardia) must demonstrate the necessity and utility of additional operative aids, such as splenectomy for the splenopathic genesis of the varix, the application of a liver fontanel or superficial hepatostomy, gastrostomy for shunting out the esophagus, hepatopexy plus omentopexy, the elimination of all cases of periportal causes of compression, and detoxicating cecostomy for elimination of the toxically acting blood within the interior of the gut.

As esophageal hemorrhage, especially in young individuals, may be the first and only indicator of cirrhosis of the liver, the timely demonstration of the varicose origin of the hemorrhage becomes necessary for diagnostic purposes and it will be of surgical aid.

(C. Henschen). Louis Neuwelt, M.D.

Marshall, S. F.: Carcinoma of the Esophagus: Successful Resection of Lower End of Esophagus with Reëstablishment of Esophageal Gastric Continuity. *Surg. Clin. North Am.*, 1938, 18: 643.

Carcinoma of the esophagus is characterized chiefly by its inoperability and by its high mortality. Generally the level at which most carcinomas occur is influenced apparently by points of narrowing in the esophagus. These points of narrowing are at the cricoid, at the aorta and left bronchus, and at the diaphragmatic opening. The symptoms usually consist of difficulty in swallowing, regurgitation of food, which may be blood stained, or the presence of substernal pain.

Ewing has pointed out that early and extensive metastases are likely to occur because of the abundant blood and lymphatic supply and because of esophageal movements resulting from swallowing. Early diagnosis is essential if operation is to be successful, and any history of dysphagia warrants careful fluoroscopic examination and esophagoscopy; a biopsy of the tumor can be performed to obtain a specimen for microscopic confirmation, and is essential for establishing the diagnosis.

The surgical removal of carcinoma of the lower third of the esophagus is influenced by the inaccessibility of the lesion and, too frequently, by the extension to the surrounding structures due to late diagnosis. In the majority of cases the advanced nature of the disease will permit the employment of only palliative measures, such as dilatation of the malignant stricture, intubation of the esophagus, or gastrostomy. In the event esophagectomy is not possible, gastrostomy should not be postponed until swallowing is impossible and until a grave state of malnutrition has developed. The mortality in late palliative operations may be very high.

A man, aged forty-six years, came to the Lahey Clinic in Boston because of pain in the epigastrium

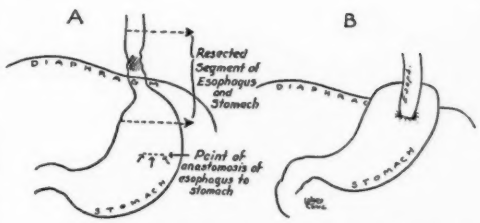


Fig. 1. A, Illustrating portion of stomach and esophagus containing tumor to be resected. B, The divided end of stomach has been inverted. The esophageal stump is transplanted into the anterior wall of the stomach, forming a new opening of the esophagus into the stomach. The incision in the diaphragm is closed about the stomach, which is partly intrathoracic.

which extended through to the back when he swallowed solid foods. The symptoms were of nine months' duration. Roentgenological examination had revealed an obstruction at the lower end of the esophagus and microscopic examination of a specimen obtained from the tumor through an esophagoscope showed it to be an adenocarcinoma.

A successful resection of the lower portion of the esophagus and the upper third of the stomach was carried out, with anastomosis of the remaining part of the esophagus to the anterior wall of the stomach after the stomach had been pulled partly into the thoracic cavity to take the place of the resected esophagus. With the patient in the left lateral position, a long infrascapular incision was made on the left side parallel to the ninth rib, the trapezius was divided, the scapula elevated, and the ribs were exposed. The entire length of the exposed ninth rib was excised; sections were removed near the proximal ends of the eighth and tenth ribs and the pleura was opened. The lung was retracted and the inferior pulmonary ligament divided. The left phrenic nerve was identified and injected with novocain in order to abolish the movement of the left half of the diaphragm. The pleura over the esophagus was incised and the esophagus exposed. The diaphragm was then opened by a radial incision extending from the esophageal hiatus to the costal margin, the peritoneal cavity being entered in this manner. The stomach was brought up partly into the thorax and mobilized by dividing the left gastric artery and other vascular attachments along the lesser curvature. The greater curvature was also mobilized by division of its vascular attachments, both curvatures being carefully cleaned off. The mobilization of the esophagus was then completed and the tumor was readily palpated at the lower end of the esophagus. The point of division of the stomach was selected and two Payr clamps were applied about 7.5 cm. distal to the lesion and including about one-sixth of the upper part of the stomach (Fig. 1). Double clamps (Ochsner) were then applied to the esophagus about 3 or 4 cm. above the lesion, a division was made between both pairs of clamps,

and the tumor was removed. The open end of the stomach was closed by over-and-over catgut stitches and inversion obtained by a second row of catgut stitches, reinforced with interrupted silk stitches. The stump of the esophagus was then transplanted into the anterior wall of the stomach through an incision placed several centimeters below the point of division of the stomach. The anastomosis was completed by an inner mucosal layer of interlocking catgut re-enforced by serosal stitches of interrupted silk. This anastomosis appeared to be entirely satisfactory and the stoma would easily admit one finger. The edges of the incision in the diaphragm were approximated to the stomach inferior to the anastomosis, the stomach was placed partially in the intrathoracic region, and the incision in the diaphragm was closed so there would be no possibility of the herniation of abdominal contents into the pleural cavity. This suture raw was re-enforced by interrupted stitches of silk. A catheter was placed in the thorax through a stab wound, sutured to the posterior parietal pleura, and attached to a constant suction apparatus for drainage. The thoracic wound was then closed.

Microscopic study of the tumor revealed that the lesion was an adenocarcinoma with metastasis to two of five lymph nodes. Blood transfusions were administered during and following the operation. Convalescence was stormy for the first twenty-one days after the operation and the patient required repeated bronchoscopic examinations in order to remove the mucous accumulation in the air passages. Eleven days after operation spontaneous rupture of the wound occurred and secondary closure was necessary, and was safely accomplished.

The patient was dismissed from the hospital on the fortieth day; the wound was healed and he was feeling comfortable. He was able to swallow satisfactorily and was taking five feedings daily.

Following dismissal from the hospital, he was seen at intervals. He had some difficulty with a choking sensation which was present at all times and not aggravated by swallowing. Esophagoscopy was performed because of persistent esophageal obstruction. The upper part of the esophagus was found to be dilated and inflamed. The esophageal opening into the stomach was about 1 cm. in width and did not dilate readily. After dilatation, the patient experienced relief and was able to swallow satisfactorily. He was last seen in the clinic seven months after the operation at which time he was able to swallow quite well but complained of some pain in his chest. JOSEPH K. NARAT, M.D.

MISCELLANEOUS

Lanzillo, F.: Surgery of the Diaphragm. I. Surgical Anatomy (Chirurgia del diaframma. I. Anatomia chirurgica). *Rassegna internaz. di clin. e terap.*, 1938, 19: 512.

The author presents a detailed review of the anatomy and surgical relationships of the diaphragm. He no longer believes that this structure simply divides the abdomen from the chest. He rather believes it to be one of the important structures in what might be called the thoraco-abdominal portion of the body, as represented by the portion between two hypothetical horizontal lines, one marking the lower level of the diaphragm, the other, the upper level. A. LOUIS ROSI, M.D.

SURGERY OF THE ABDOMEN

GASTRO-INTESTINAL TRACT

Persson, M.: Postoperative Phlegmonous Gastritis (Gastritis phlegmonosa postoperativa). *Acta chirurg. Scand.*, 1938, 80: 497.

Resection of the stomach and duodenum plus gastro-enterostomy, Billroth II, were undertaken on a female patient, forty years of age, with medically intractable ulcer of the duodenal bulb. Healing was uneventful and the patient was discharged two and a half weeks later. The next day, after returning home, fever, sore throat, and prostration of influenzal character developed, and two days later vomiting occurred and pain was present in the right lower quadrant. The appendix at removal, twenty-two days after the resection, exhibited some pathological changes and there was some seromucous fluid in the peritoneal cavity, but palpation of the upper abdominal cavity through the operative incision failed to reveal any evidence of abscess.

Following appendectomy the condition of the patient became worse and two days later, under a tentative x-ray diagnosis of subphrenic abscess, the eleventh and twelfth ribs on the left side were resected, and a large abscess, bounded by the stomach, spleen, left lobe of the liver, and diaphragm, was uncovered and drained. The stomach at this operation was swollen and thickened, and at autopsy the following day the gastric wall was found to be greatly thickened and interpocketed with turbid grayish-yellow pus. Culture revealed the streptococcus. The course of the condition was as follows: phlegmonous gastritis, subphrenic abscess, and then diffuse purulent peritonitis.

This case, in view of 2 others reviewed by the author from the literature, 6 collected by Finsterer and 4 by Perman (*Acta chirurg. Scand.*, 1935, Supp. 38, in English), is the thirteenth reported instance of postoperative phlegmonous gastritis. The author accepts in the main the conclusions of Perman, even believing that the peculiarities of this case strikingly support that author's views as to the pathogenesis of the condition.

The long, complication-free interval following the resection renders the subsequent development of a nascent phlegmonous process unlikely, but the toxins of the anginal process would explain the presence of a hypo-acidity favoring prevalence in the stomach of virulent swallowed bacteria, which might invade the gastric wall by way of the sluggishly healing mucosal stratum of the suture line at the gastro-intestinal junction, resulting from the first operation.

As practical conclusions the author suggests the importance of pre-operative mouth hygiene and of the shielding, in so far as possible, of the patient recently operated for ulcer from infections of the respiratory tract. JOHN W. BRENNAN, M.D.

Didier, R., and Bompart, H.: The Treatment of Ulcer Situated High on the Lesser Curvature by Gastrectomy in Two Stages (Le traitement de l'ulcère haut situé de la petite courbure par la gastrectomie en deux temps). *J. internat. de chir.*, 1938, 3: 451.

The authors devised a two-stage operation for ulcer situated high on the lesser curvature in order to avoid the leakage at the suture line which frequently occurs following resection of the stomach in patients having a peptic ulcer of the cardia. In the first stage a gastro-enterostomy is performed without invasion of the inflamed ulcer area, and in the second stage, which is done after the gastro-enterostomy has healed, essentially a gastric resection is done.

The authors believe that this two-stage operation lowers the mortality by reducing the tendency toward leakage of the gastrojejunal suture line. The operative technique consists of first freeing the greater curvature of the stomach and placing a clamp as shown in Figure 1. Then a retrocolic gastrojejunostomy is made as shown in Figures 2, 3, and 4. This gastrojejunostomy is really an end-to-side anastomosis. A triangular stomach segment, the base of which is the greater curvature, is resected at this time, and the lesser curvature containing the ulcer is left undisturbed. From four to six weeks later the rest of the stomach is resected, at which time the original lesion is much smaller.

The authors also believe that this operative technique is simpler. In a series of 20 cases they

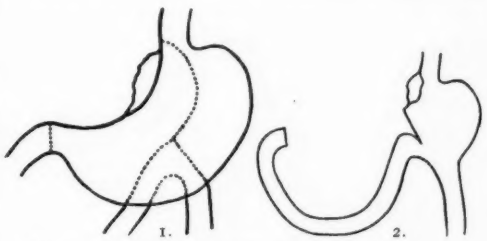


Fig. 1. Grooved gastrectomy of Pauchet.
Fig. 2. Procedure of Wells.

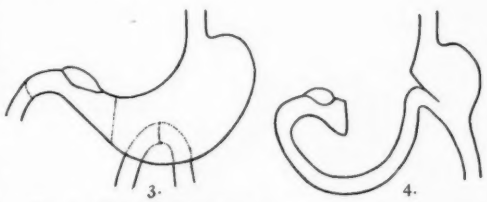


Fig. 3. Ancient pylorectomy.
Fig. 4. Resection by exclusion according to Finsterer.

have found this two-stage operation very satisfactory. SAMUEL J. FOGELSON, M.D.

Bonne, C., Hartz, P. H., Klerks, J. V., Posthuma, J. H., and Others: The Morphology of the Stomach and Gastric Secretion in Malays and Chinese, and the Different Incidence of Gastric Ulcer and Cancer in These Races. *Am. J. Cancer*, 1938, 33: 265.

The low incidence of gastric ulcer and carcinoma among Malays as contrasted to the incidence among the Chinese living in Java has been previously reported, but no definite attempt has been made to explain the difference. A few speculative theories have been advanced. The diet of the Malay is much more vegetarian in character than that of the Chinese, but this general statement cannot be taken as a starting point for a serious investigation because there are no analogous observations among other groups of individuals living largely on a vegetarian diet. The same criticism arises with regard to the difference in consumption of alcoholic beverages, which consumption, as a rule, is lower among the Malays than among the Chinese. The Malays, who are almost all Mohammedans, do not eat pork. This cannot be a factor because many Jews exclude pork from their diet and still neither gastric carcinoma nor gastric ulcer is less prevalent among them than among gentiles. The absence of physical emotion is characteristic of the Malay race. This has been suggested as a possible influence of the anatomical nervous system on the formation of ulcer. When this phase of the subject was investigated with Danielopolu's atropine test, no definite preponderance was found in either race.

In 951 Chinese autopsies, 28 gastric and 17 duodenal ulcers were found. In 2,312 Malay autopsies, 8 gastric and 12 duodenal ulcers were found.

This study first concerned itself with detailed histological findings of the stomach. The stomachs of the two races showed grossly little or no difference in size. Histologically, the distribution of glands was also found for practical purposes to be the same. From a detailed careful study, the authors concluded that although there was a great difference between gastric pathology of the Chinese and that of the Javanese with regard to the major lesions, such as gastric carcinoma and gastric ulcer, the minor lesions also demonstrated an interesting finding.

Chronic atrophy, gastritis, and goblet-cell metaplasia were also distinctly higher among the Chinese than among the Malays, but generalized gastritis and erosions were more or less equally frequent in both races. "The rarity of gastric ulcer in the Javanese is due not to relative absence of erosions but to the absence of some deleterious factor that in Europeans and Chinese leads to ulcer formation on the basis of erosion."

Further studies on gastric secretion which involved acid values, pepsin content, total base, sodium, potassium, calcium, magnesium, chlorine, emptying time, and plus nitrogen showed little or no difference, except with regard to the nitrogen values, which were somewhat higher in the Chinese.

Summarizing these findings we may be tempted to conclude that in the pathogenesis of ulcer there are two stages. The first, in which atrophic gastritis and the formation of superficial erosions are present, occurs equally frequently in both races; but the second, or the destructive process, is arrested in the Javanese by some unknown factor, and the formation of true ulcer is prevented.

SAMUEL J. FOGELSON, M.D.

Scott, H. G.: Intestinal Obstruction: Experimental Evidence on the Loss of Blood in Intestinal Strangulation. *Arch. Surg.*, 1938, 36: 816.

Numerous attempts have been made in the past to ascribe the disastrous effects of all types of intestinal obstruction to some one etiological factor. Of the numerous explanations offered, that of intestinal toxemia has been given the greatest consideration. Hundreds of investigators have attempted to put the blame on this or that toxin as being directly responsible for the dire results. There was never at any time any agreement as to what toxin was responsible. Moreover, the fact that no theory of intestinal toxemia has ever offered any benefit to the patient in the way of improved methods of treatment or lowered mortality has cast grave doubt on this explanation. However, so firmly has the theory of intestinal toxemia become rooted in the consciousness of medical practitioners that the concepts advanced in more recent years have been but slowly and hesitatingly accepted.

During the past thirty years investigators have shown, anatomically and pathologically at least, that intestinal obstruction may be divided into two major types, or a combination of the two. Clinicians and investigators alike have used the terms "simple obstruction" and "strangulation obstruction" to designate and differentiate the two major forms. Of recent years such investigators as Wilkie, Murphy, Elman, Scott, Blalock, and Mensing have called attention to the fact that the loss of blood in intestinal strangulation may be of some consequence in bringing about and aggravating symptoms of shock and in causing death. Wilkie, in 1913, clearly distinguished between simple and strangulation obstruction. He was impressed with the amount of blood lost in strangulation obstruction and believed that it played an important rôle in the causation of shock and death. While conducting some experiments on strangulation obstruction in the dog, the author observed significant loss of blood into the walls and lumen of the strangulated bowel. The present paper by the author is the outcome of further experiments which he conducted in order to determine the extent of the loss of blood and its relation to changes in the blood pressure, shock, and death as seen in these conditions. In this paper the results of 240 experimental strangulation obstructions are presented.

Before proceeding with the subject matter of these experiments, it might be well to refer briefly to the terminology used. The term "simple obstruction" refers to the occlusion of the lumen of the bowel without gross interference with the mural blood supply. The term "strangulation obstruction" implies a vascular impairment of the wall of the bowel and its mesentery. The author points out that at operation or autopsy, patients for whom the diagnosis was made clinically not infrequently showed some evidence of both types of obstruction. Most strangulation obstructions are accompanied by a simple mechanical or neurogenic obstruction. Because of a rather frequent combination of simple and strangulation types, with their overlapping syndromes, many patients observed clinically fail to present typical symptoms of either type of obstruction. Consequently, the surgeon and clinician find it rather difficult to realize that two entirely different physiopathological processes might be responsible for producing the many complex effects of intestinal obstruction.

The author ingeniously employed four methods in producing the experimental strangulation obstructions recorded in this paper, in order to make it possible to evaluate the rôle that the arteries and veins may play, individually and collectively, in determining the period of survival of dogs with strangulation obstruction. In his first method a partial occlusion of lumen and blood supply was employed. This group represented obstruction by encirclement only. In the second, there was complete arteriovenous obstruction. The third featured complete arterial obstruction with a patent vein; while the fourth featured complete venous occlusion with an intact artery. These four methods make possible an interesting comparative study.

The author gives a detailed account of the pathological and microscopical findings of each group and lists the results in tabulated form. Naturally, marked differences were noted in the various groups. The gross pathological picture, as well as the microscopic observations in all instances, however, indicated a loss of whole blood in the wall and lumen of the strangulated loop of the bowel. It was found that the relative degree of venous or arterial occlusion determined the type of strangulation produced. With venous occlusion predominating, the loss of whole blood was the chief factor. With arterial occlusion predominating, the loss of plasma was important.

Increase in the weight of the strangulated bowel over the normal weight was likewise observed by the author. This increase in weight was shown to be due to the accumulation of blood in the wall and lumen of the strangulated loop of the bowel. Further observations showed that the hemoglobin content of the material within the loop was high and that the free peritoneal fluid was similar in total protein content to the animal's own blood plasma.

The author was able to calculate the loss of blood in strangulation obstructions. This loss of blood, in the venous types of occlusion at least, was found adequate to account for the shock and death of the experimental animal. Experiments in these instances tended to show that the blood pressure falls rapidly and the hemoglobin content drops rather uniformly.

Furthermore, the author established the fact that there was a definite correlation between the fall in the blood pressure and the time, length, and type of intestinal strangulation. In general, the longer the time and the longer the loop strangulated, the greater was the fall in the blood pressure. The type of obstruction, however, was of even greater importance. In those instances in which the veins alone were ligated, and in the strangulations involving encirclement in which the arteries were not entirely occluded, the fall in pressure was much more rapid than in those instances in which the arteries were absolutely occluded, with or without occlusion of the veins.

Additional experiments were presented to demonstrate that "toxic products" are not present in the peritoneal fluid except terminally when the loops are gangrenous or ruptured. In view of the controversy concerning the absorption of so-called "toxic products" from the obstructed bowel, it was deemed advisable to test the absorptive power of the normal and of the strangulated intestine for products of known toxicity. Histamine, strychnine, and tetanus toxin were introduced into strangulated loops (the usual four types of strangulation were employed) in order to test the absorption of these products. Careful experiments were carried out to make a complete check-up from this angle. Practically all the tests failed to reveal any evidence of absorption of these products, except terminally, when the loops were gangrenous or ruptured.

Later experiments were carried out which tended to show that the intestinal wall *per se* is not toxic. In order to determine whether the wall of the bowel itself was "toxic," an attempt was made to free the normal intestine of the dog from its usual bacterial flora by chemical and thermal sterilization. Segments of bowel thus treated were placed in the peritoneal cavities of normal dogs, in order to determine their relative and actual degree of "toxicity," as judged from a clinico-experimental standpoint. These experiments substantiated the experimental results of other investigators, notably Dragstedt and his co-workers, who showed that it was extremely difficult to sterilize the normal bowel with the usual antiseptics. Careful bacteriological studies were then conducted and these tended to show that the only evidence of toxic absorption was found late in the course of any strangulation obstruction and was apparently due to the presence of innumerable bacteria in the peritoneal cavity. The author observed that the effect of the bacteria was apparently quantitative, as gross perforation of the intestine was essential to a lethal issue when the peritoneal fluid was tested by introducing it into the peritoneal cavity of a normal animal.

The author draws some interesting conclusions from his experiments which are of great significance. In the first place, strangulation obstruction, like intestinal obstruction in general, is not a distinct disease. To quote the author, "The train of symptoms, the development of shock and finally the ensuing death depend on at least three factors:

1. Loss of blood into the wall of the bowel, the lumen and the peritoneal cavity.
2. Transudation of plasma into the general peritoneal cavity.
3. Absorption of bacterial toxins.

The course taken in any strangulation will depend on the relative degree of venous or arterial occlusion. If arterial occlusion predominates, the resulting pathologic picture will be an anemic or hemorrhagic necrosis without marked distention of the lumen or the wall of the bowel. In these instances there will be an outpouring of plasma from the surrounding peritoneal surfaces in an attempt to rid the peritoneum of the gangrenous bowel. Death will occur relatively late and will be secondary to a loss of plasma into the peritoneal cavity and an absorption of bacterial toxins therefrom. If, on the other hand, the venous occlusion predominates in the face of normally patent, pumping arteries, or even partially patent arteries, the result will be a loss of whole blood into the wall and lumen of the bowel and a transudation of plasma into the peritoneal cavity, associated with a distention of the strangulated loop, varying from a moderate to a marked degree."

From these observations it seems quite plausible to add that whole blood and plasma are apparently lost from the general circulation in quantities sufficient in themselves to account for the symptoms of shock and death which occur in most cases of strangulation obstruction. MATHIAS J. SEIFERT, M.D.

Donaldson, J. K.: Intestinal Obstruction. An Analysis of 200 Cases Attempting Improved Correlation of Mortality, Pathological Physiology, and Signs and Symptoms. *Am. J. Surg.*, 1938, 40: 505.

In a recent discussion of intestinal obstruction the author stressed various morbid processes of the disease as they occur in different conditions ordinarily listed under the title of intestinal obstruction. He presented a simplified classification based upon pathological physiology. The chief efforts made in this present article are to analyze mortality rates and signs and symptoms in different types of obstruction with appreciation of the distinction between early and late signs.

The total mortality for all cases of intestinal obstruction was 58.8 per cent. The folded loop obstructions are more serious than the simple ones and the mortality was 71.4 per cent. In the simple obstruction, the mortality was 59 per cent. In 2 cases of mesenteric thrombosis the mortality was 100 per cent. In 3 cases of intussusception the mortality was 50 per cent. The seriousness of cases of gangrene was demonstrated by a mortality of 100 per cent.

One must remember that the interference with the arterial blood supply leading to gangrene gives the most fulminating picture in obstruction. Loss of salts is also an important factor but one which is easily combated. Distention may be a lethal factor in obstruction in that it may cause an ischemia of the mucous membrane, allowing toxins to be absorbed. Loss of essential salts and fluids is likely to be more rapidly serious in obstructions which are situated high in the small gut than in lower large-bowel obstructions.

The most reliable finding in direct lumen obstruction is available through the use of x-rays. Gas and fluid levels in the small bowel become characteristic in from three to six hours. Fluid levels will occur in direct lumen obstructions as in paralytic ileus. Under late signs and symptoms may be included distention, decreased peristalsis, marked rigidity (peritonitis), and shock with collapse.

JOHN W. NUZUM, M.D.

Berman, J. K.: Duodenogastric Intussusception: Its Clinical Application and Results. *Arch. Surg.*, 1938, 37: 139.

Berman made experimental duodenogastric intussusceptions in dogs by incising the pyloric sphincter longitudinally and then invaginating the pars superior duodeni into the pyloric antrum. He found that the invaginating portion remained in place for many months and showed no morphological changes. A procedure of this type places the ulcer-bearing area, which consists of the pyloric end of the stomach and the first part of the duodenum, into a new environment which is more highly acid.

A study of the animals prepared in this manner showed that Brunner's glands have two secretions: (1) a local protective mucin, and (2) a systemic acid-stimulating hormone. It was also shown that hydrochloric acid stimulates the local production of mucin as well as of gastrin, and the production of the latter, in turn, leads to the secretion of hydrochloric acid, the cycle thus being perpetuated. It was also seen that the adventitious duodenal mucous membrane in these experimental animals showed no ulceration despite exposure to increased acidity and the rapid emptying time. The defensive mechanism afforded by the excess mucin secretion was believed to be the protecting factor.

The operation devised by the author has been tried clinically on 5 patients. The first patient was operated upon for a perforated duodenal ulcer of the anterior wall on February 2, 1936. The hepatogastric, hepatoduodenal, and gastrocolic ligaments were divided up to the upper portion of the pyloric antrum and down to a point 1¼ in. below the pylorus, this portion of the stomach and duodenum thus being mobilized, and the pyloric sphincter was divided longitudinally down to the mucous membrane. The duodenogastric intussusception was then accomplished, and the greater omentum placed over the operative field. The patient has remained well to date.

In addition, 4 other patients were operated upon. One patient had a large gastric ulcer of the lesser curvature, the second a postpyloric duodenal ulcer on the lesser curvature, the third a duodenal obstruction secondary to duodenal ulceration, and the fourth a large duodenal ulcer of the posterior wall which was adherent to the pancreas. The response to surgery was very satisfactory in all of these patients. They presented acid values which remained either within the normal limits or were slightly lower, but the mucin content of the gastric secretions was 2.2 mgm. per c.cm. as contrasted to the normal averages of from .4 to .7 mgm. which were previously reported by Anderson and Fogelson.

SAMUEL J. FOGELSON, M.D.

Cutler, C. W., Jr.: Changing Methods in the Surgical Treatment of Peptic Ulcer. *Ann. Surg.*, 1938, 108: 68.

The various changes leading to the present routines utilized for the treatment of ulcer in the Roosevelt Hospital, New York, are summarized by the essayist.

As early as 1907 Brewer reported 17 cases operated upon by him at Roosevelt Hospital. At that time he deplored the inadequacy of diagnostic methods and treated "simple round ulcer" medically for six weeks. After this period surgery was advised if the patients were "unrelieved." Between 1912 and 1914, Brewer and Cole proceeded to improve their diagnostic technique so that they were able to make accurate diagnoses in 89 per cent of the cases. This diagnostic aid led to greater activity on the part of the surgeons of the Roosevelt Hospital.

In 1915 Peck reported 134 operations on the stomach for benign lesions performed at the Roosevelt Hospital between 1910 and 1915. He pointed out that gastro-enterostomy was the routine treatment for chronic duodenal ulcer, having been performed in 72 of 74 cases with a surgical mortality of 8.1 per cent. From 58 of these cases which could be traced subsequently he estimated that 68.9 per cent of all the patients who were operated upon were cured.

Over the period of ten years from 1917 to 1927, the number of surgical interventions for duodenal ulcer increased. Four hundred and twelve gastro-enterostomies were performed. At this time the surgeons believed that peptic ulcer was essentially a surgical disease and that the surgical treatment was in the main satisfactory. However, as early as 1924, Peck had reached the conclusion that these patients should have a thorough and intelligent trial of medical treatment before surgery was considered. At this time he reported on 196 cases of chronic duodenal ulcer in which he performed 191 gastro-enterostomies. The surgical mortality was 8 per cent. Even then Peck made mention of the fact that resection was being considered after primary gastro-enterostomy in the more severe cases. He believed that "routine resection is not indicated. . . . We do not believe that gastro-enterostomy should go into discard in the treatment of duodenal ulcer, nor do we believe that extensive resections of the normal stomach are justifiable for this lesion. We are unconvinced that resection to prevent the formation of gastrojejunal ulcer is a proper procedure for the 98 cases who do not need it to possibly avoid its occurrence in the other 2."

Peck's report from 1924 to 1937 showed that at the Roosevelt Hospital 262 operations for chronic ulcer of the stomach or duodenum, exclusive of operations for acute perforations of primary ulcer, were performed. "It is of interest to note that year by year the number of operations performed for this condition has gradually diminished and this without a significant diminution of the number of cases admitted." In 1926 there were 46 such operations, whereas in 1936 there were but 12.

It is now the practice at the Roosevelt Hospital to consider all cases of chronic peptic ulcer as medical problems and Cutler agrees with Oschner, who says, "It is our firm conviction that there is no surgical treatment of peptic ulcer and that surgery is indicated only when there are complications." No patient is now operated upon at Roosevelt Hospital for chronic peptic ulcer without having had a thorough controlled and efficient course of medical management. In each case in which operation is proposed, this action must be approved by a court consisting of physician, surgeon, gastro-enterologist, and roentgenologist. The criteria for surgery are:

1. Persistence of pain in spite of a trial of adequate medical management.
2. Persistent or recurring pyloric obstruction.
3. Massive recurrent hemorrhage in which fatality is feared.
4. Recurrent hemorrhage even if the symptoms are controlled by treatment.
5. A lesion of the stomach which appears intractable to adequate treatment or suggests the presence of malignancy.

The selection of the type of surgical intervention has shown a slow but definite change. The number of gastro-enterostomies has been slowly decreasing year by year whereas the resection type of operation has shown a gradual increase. This change is probably due to the fact that the patients not benefiting from medical therapy are those with scarred or sclerosed ulcers, ulcers penetrating the head of the pancreas, ulcers invading the blood vessels, ulcers which have caused duodenal or pyloric obstruction and occurred when the motor and secretory activity was marked and when the recurrence of ulcer was likely to be high. Chronic gastric ulcers are also treated by resection when the risk is not too great for the patient, because resection discourages the tendency toward recurrence and diminishes the probability of advancing malignancy, should there be any suspicion of cancer.

The mortality rate for resection in the last fourteen years has been 9.3 per cent as contrasted to the 8.5 per cent mortality of gastro-enterostomy during the same period. However, when one considers the 16 per cent of late poor results from gastro-enteros-

tomy as against the 3 per cent of poor results from resection, this slight increase in mortality is negligible.

In summary, at the Roosevelt Hospital, New York, the tendency has been to decrease the number of surgical interventions, but if surgical intervention is selected it is generally of a more radical type. SAMUEL J. FOGELSON, M.D.

Chamberlin, D. T.: Malignant Tumors of the Small Intestine. *Surg. Clin. North Am.*, 1938, 18: 705.

Malignant tumors of the small intestine may be classified according to their gross characteristics into annular and asymmetrical tumors. The carcinomas are usually annular, while sarcoma tends toward the expansive type of growth.

The diagnosis of malignancy of the small bowel is not often made before operation or post mortem; the extreme rarity of the condition discourages diagnosis. Rowe and Marshall found reports in the literature of 339 tumors of the small bowel, of which 38 (4.9 per cent) were malignant. Ackman reported 600 cases of intestinal carcinoma in the Montreal General Hospital, of which only 7 were true carcinomas of the small intestine.

If carcinoma of the ampulla of Vater is included, the duodenum leads as the most common site of carcinoma of the small bowel. The jejunum is next in frequency and the ileum last. The average age of all patients whose cases have been reported in the literature is from forty-five to fifty years. The symptomatology varies with the size and character of the tumor and its position in the small intestine. The closer it is to the pylorus, the more acute the symptoms are when obstruction sets in. The duration of symptoms may be as short as two months or as long as five years, depending upon the character and position of the tumor. Carcinoma which occurs proximal to the ampulla of Vater produces symptoms that are in no way different from those present in pylorus obstruction due to any other cause. Cancer of the ampulla itself produces painless, uninterrupted, obstructive jaundice, and dilation of the gall bladder, and cannot be distinguished clinically from carcinoma of the head of the pancreas. Cancer occurring distal to the ampulla in the duodenum and upper jejunum results in slowly progressive obstruction with severe cramplike epigastric pain, at its peak two or three hours after meals.

Tumors in the jejuno-ileal region make themselves known by two groups of symptoms. In the first group there are vague symptoms, fairly constant and progressive. Malaise, anorexia, and weight loss are usually present; anemia is a frequent symptom. The pain is shifting, dull, and cramp-like in character. As the lumen of the bowel is encroached upon, vomiting once or twice a week may occur, with partial relief of the symptoms. One type of malignant tumor does not obstruct, but grows away from the lumen of the bowel. In such cases the only finding will be a hypochromic anemia, until the mass grows large enough to be palpable.

The prognosis of carcinoma of the small bowel is generally poor. The cancer has a tendency toward early metastasis to the mesenteric lymph nodes, peritoneum, liver, lungs, bones, and spinal dura, in the order named. X-ray findings often make a diagnosis possible only after metastasis has taken place. Kiefer gives the average duration of life after resection as one year, and in his report of a series of 11 cases of malignancy of the small bowel there was only 1 patient alive five years after a resection for carcinoma of the jejunum.

The treatment is entirely surgical, and the most difficult part of the problem is to recognize the lesion early enough for a hopeful prognosis.

During the past five years there have been 11 cases of malignant tumor of the small intestine, of which only 4 were diagnosed as such before operation. Six patients were found to have carcinoma, and 3 lymphosarcoma. All 9 patients were operated on for obstructive symptoms. The 3 cases of lymphosarcoma were all in younger patients. The earlier appearance of lymphosarcoma is frequently noted in the literature. The lymphosarcomas take a very rapid course so that there is not time for the development of a profound anemia before obstructive symptoms supervene. The x-ray examination of the small intestine is carried out by means of a barium meal on a fasting stomach and films of the abdomen taken at hourly intervals for six hours. The author reports 9 cases of malignancy of the small bowel which came to operation in the Lahey Clinic, Boston.
JOHN W. NUZUM, M.D.

Bower, J. O., Burns, J. C., and Mengle, H. A.: The Bacteriology of Spreading Peritonitis Complicating Acute Perforative Appendicitis. *Surgery*, 1938, 3: 645.

The authors review the literature on the bacteriology of peritonitis of appendiceal origin, with particular reference to the significance of the gas-producing anaerobes in the pathogenesis of this disease. They obtained exudate from 55 cases of "gangrenous appendicitis with spreading peritonitis." This material was transferred to media and incubated aerobically and anaerobically. Phosphorous combustion was used for the production of anaerobiosis. Anaerobic cultivation was performed only on material which had been heated to 80° C. for fifteen minutes to destroy the non-sporeforming bacteria, which method prevented, of course, the identification of non-sporulating anaerobes, such as the anaerobic streptococci, and also those anaerobes which form spores in media but not in the body.

The percentage incidence of individual organisms in relation to the total series is not reported, but the proportion of total positive aerobic or anaerobic cultures in which the organism was found is indicated.

In this series, colon bacilli were found in 50 per cent of the cases, streptococci of various types in 25 per cent, and clostridium welchii in about 26 per cent.

The authors also studied the bacterial flora of induced peritonitis in dogs and, according to the statistical method used, found that the incidence of clostridium welchii in this lesion was similar to that in human peritonitis. Organisms found in lesions of living dogs are compared with the flora in dogs dying of peritonitis. The incidence of bacillus coli infection appeared to be considerably higher in human peritonitis than in dog peritonitis.

The authors mention briefly their conviction that the strains of clostridium welchii encountered were actively pathogenic and contributed to the toxemia of the peritonitis, but they state that the complete data on this point will be published in a separate paper. JOHN S. LOCKWOOD, M.D.

Cave, H. W.: The Surgical Treatment of Intractable Chronic Ulcerative Colitis. *Ann. Surg.*, 1938, 107: 806.

The permanent cure of extensive intractable chronic ulcerative colitis demands the complete removal of the diseased bowel. Less radical measures have proved inadequate. Medical management, which has consisted principally of rest in bed, a caloric-high-vitamin and low-residue diet, irrigations, the elimination of focal infections, and the use of vaccine and serums, has for the most part, been ineffectual. The percentage of lasting or permanent cures has been exceedingly small; therefore colectomy, partial or total, is a measure of necessity.

The indications for surgery are discussed. Apart from the acute emergencies of impending perforation or massive repeated hemorrhage, surgical treatment should be withheld until two factors have been evaluated: the clinical response to conservative treatment, and the degree and extent of permanent damage to the colon. Failure to achieve definite clinical improvement by the various conservative measures, persistence and progression of the lesions as seen at proctoscopy, and roentgenological evidence of progressive fibrosis of the colon with pseudopolypoid degeneration of the mucosa constitute the elective indications for surgery.

Appendicostomy, cecostomy, and colostomy are considered by the author to have no place in the management of intractable chronic ulcerative colitis. In his experience, these procedures are not curative or even palliative, and they complicate subsequent radical surgery when and if this becomes necessary. Partial colectomy is justified in well selected cases in which the disease is definitely limited to one portion of the colon; the Mikulicz type of resection is ideal and relatively safe. If the rectum and lower sigmoid are involved alone, a combined abdominoperineal resection in two stages will minimize the complication of peritonitis.

Ileostomy as a curative measure has been discarded. Diversion of the fecal current may produce a striking clinical improvement, yet the toxemia, although temporarily diminished, persists and the patient is not cured until the infected colon is removed.

Colostomy is of value in diverting the fecal stream, particularly in cases in which only the lower sigmoid and rectum are involved, and in many instances assures the patient of less inconvenience than ileostomy.

Ileosigmoidostomy, preferably end-to-side, as a first-stage measure prior to subtotal colectomy has been successfully utilized; however, there is grave danger that by such a measure the disease process may extend into an otherwise healthy rectum. The author emphasizes the fact that it is only in an exceedingly small group of cases (less than 10 per cent) of segmental colitis that ileosigmoidostomy is ever justified. He considers it important to state clearly that this procedure is unwarranted if the descending colon and rectum show the slightest involvement.

The entire diseased large intestine can be removed without great risk. Pre-operative preparation is important and must be carefully and thoroughly carried out. Repeated small transfusions are suggested; also adequate intravenous administration of glucose in saline, colonic irrigations with warm saline solution, low residue or non-residue diet, and the administration of lead and opium.

Three separate stages (occasionally four) are usually required to perform a total colectomy.

First stage: Transverse permanent ileostomy 6 in. from the ileocecal valve through a right McBurney incision. The distal end of the divided ileum is dropped back into the abdominal cavity; if stricture of the colon exists, it is preferable that a mucous fistula of the distal divided end be established.

Second stage: At least from five to eight weeks, and even more time, should elapse between the first and second stages, to insure the establishment of water balance. A long left paramedian incision is made. The small segment of terminal ileum, and the ascending, transverse, descending, and upper sigmoid colon are removed and only approximately 4 in. of the lower sigmoid above the peritoneal reflection are left. The stump may be sutured in layers, or it may prove safer to suture the open lower sigmoidostomy to the anterior abdominal wall.

Third stage: Combined abdominoperineal resection in one stage, from two to six months after the second stage, to permit of satisfactory rehabilitation.

In a few selected cases a two-stage maneuver may possibly meet the requirements. This possibility is predicated upon the proven presence of a normal sigmoid and rectum, and the first stage consists of end-to-side ileosigmoidostomy, and the second of subtotal colectomy. In cases in which the left colon and rectum alone are diseased, a two-stage procedure is all that is necessary: first, a transverse colostomy with removal down to the lower sigmoid and second, a combined abdominoperineal resection.

Occasionally, in the patient who is a particularly bad risk, four stages are safer. The second stage would then consist of removal of the ascending and transverse colon, the splenic flexure to be left in place, and then removal of the descending and upper sigmoid colon for the third procedure.

A résumé of the case histories of 6 colectomized patients is presented. In this series (carefully and frequently observed since operation) it has been found that the patients manage the ileal stoma without undue inconvenience, their mental attitude is surprisingly cheerful, and they possess a feeling of well being, due no doubt to their extraordinary gain in weight. No permanent deleterious results have been found to occur following colectomy.

JOHN H. GARLOCK, M.D.

Charrier and Goumain: Villous Tumors of the Rectum (Tumeurs villeuses du rectum). *Bordeaux chir.*, 1938, 9: 77.

Charrier and Goumain have observed 5 cases of villous tumor of the rectum. On the basis of their findings, they discuss the histology, symptomatology, and treatment of this type of tumor.

These tumors may be pedunculated or sessile; the pedicle, if present, is usually short. Or, they may occur in the form of multiple vegetations, rather than a single tumor.

When benign, these tumors never invade the muscularis mucosæ but arise from the chorion. They consist of multiple villi, lying in all directions; each villus is formed of vascular connective tissue, arising from the chorion and covered with epithelium; the epithelium shows two types of cells: dark-colored cylindrical cells and muciparous cells. The latter are similar to those found normally in the intestines, but are unusually numerous in these tumors and secrete an abundance of mucus, which covers the surface of the tumor. Malignant changes in these tumors take place very gradually; the first change noted is in the cylindrical cells, which become flatter and more cuboid; the nuclei become oval, stain less intensively, and show numerous irregular mitoses. At the same time the function of mucus secretion disappears; this was a notable feature in the authors' third case, which was the only one in their series to show malignant changes. Then the neoplastic process advances and modifies the entire architecture of the tumor, which becomes infiltrating and invades the muscularis mucosæ; invasion of the lymphatics does not occur until a later stage. There is another type of villous tumor of the rectum, the dendritic villous tumor, which does not represent a malignant degeneration of a benign tumor, but is primarily malignant; it does not arise from the superficial layers of the chorion, but from a depression in the chorion; and its epithelial cells are atypical, polymorphous, and definitely neoplastic from the first. None of the authors' cases were of this type.

The chief symptom of villous tumors of the rectum of the benign type is the discharge of mucus; this discharge is clear and slightly viscous, like the white of egg. Bleeding may occur but it is usually slight. The copious discharge of mucus, if mixed with fecal matter and causing a desire to defecate, may simulate a diarrhea; but in reality there is little if any change in the consistency of the stools and no true diarrhea.

If the tumor is benign, it causes no pain even at defecation; if pain is noted, it suggests a malignant degeneration. The general condition of the patient with a benign villous tumor is good; there is rarely enough bleeding to cause secondary anemia. The tumor can be palpated with the finger in the rectum in 80 per cent of the cases. However, it is best studied with the proctoscope, because even if it is large, it is yielding and elastic, so that it offers little obstruction to the passage of the instrument. The condition of the rectum above as well as below the tumor can be observed.

The treatment of these tumors is surgical. If biopsy has shown no signs of malignant degeneration, removal of the tumor with a margin of normal tissue gives good results. For this operation, the anus should be well dilated, and spinal anesthesia should be used if the patient's cardiovascular condition permits. As the tumors are vascular, and there is apt to be considerable hemorrhage, the authors prefer the use of the electric cutting current, as the best means of controlling the bleeding. They used this method in 3 of their cases. In 1 case there was a recurrence within seven months; this recurrent tumor showed signs of beginning malignant degeneration consisting of the absence of muciparous cells and malignant changes in the cylindrical cells, but no infiltration of the deeper tissues. In this instance a perineal amputation of the rectum was done. The authors recommend this operation only in those cases in which evidence of malignant change is found by biopsy.

ALICE M. MEYERS.

D'Allaines, F., Jourdan, P., and Stéfani, L.: Surgery of the Rectum by the Transsacral Route (La chirurgie du rectum par la voie trans-sacrée). *J. de chir.*, 1938, 51: 817.

D'Allaines, Jourdan and Stéfani note that the transsacral route for operations on the rectum (Kraske's method) has practically fallen into disuse in France; but it has certain advantages which they point out. The transsacral route gives a more direct approach to the ampulla, greater facility in the closure and suture of the peritoneum, and an easier approach to the superior vascular pedicle.

In cases in which the lower limit of the tumor is less than 4 cm. above the levator-ani muscles, an amputation and not a resection of the rectum is definitely indicated. In such cases the transsacral route has certain advantages for some of the steps of the operation, especially for the removal of the rectal sheath. In these cases a combined perineosacral method may be employed. In cases in which the lower limit of the tumor is 4 cm. or more above the levator muscles, it may be possible to re-establish the continuity of the intestines and avoid a permanent artificial anus. The Kraske method gives the much better approach when this operation is indicated. Whether it is possible can often be determined only at operation, and for that reason it is preferable to use the transsacral approach whenever there is a possibility that the continuity may be re-established.

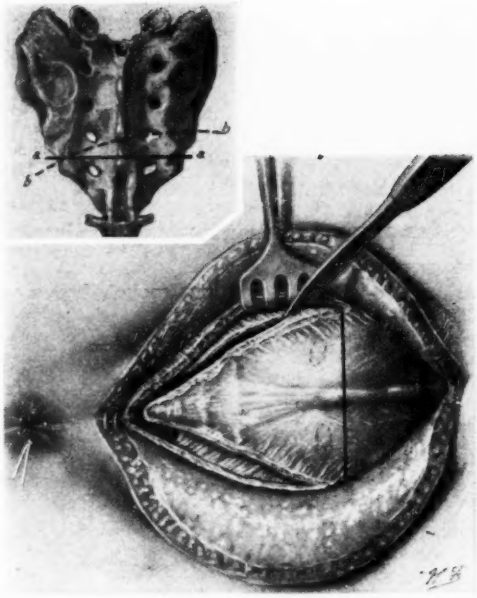


Fig. 1. Liberation of the sacrum; in the inset, the lines indicate two types of resection; (a) minimum, (b) large.

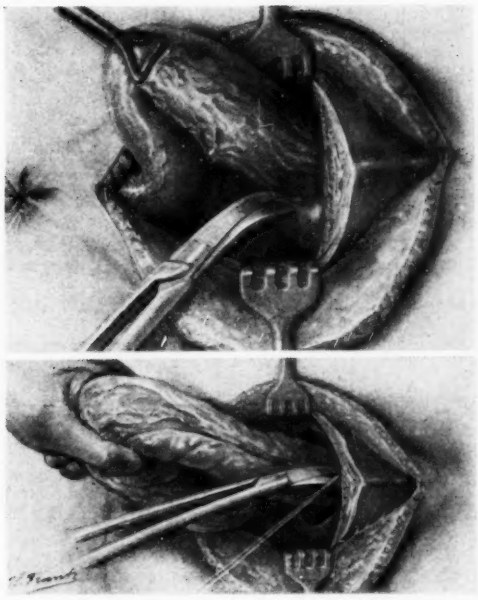


Fig. 2. Above: Opening the peritoneal cul-de-sac. Below: ligature of the superior hemorrhoidal artery.

When this is the case a temporary artificial cecal anus must be established at least three weeks before the main operation.

For the transsacral operation, the patient lies on the left side with the pelvis raised and the thighs flexed on the abdomen, giving an easy approach to the sacrum. The skin incision begins about midway between the anus and coccyx and is carried upward in a slight curve to the base of the sacrum. After section of the sacrum, the rectal sheath may be entirely removed and the upper portion of the rectum and the tumor freed and drawn out through the operative wound. The peritoneum is opened, which may present some difficulty, especially in the male and should be done at some distance from the tumor. The superior hemorrhoidal artery is then ligated. The lower part of the rectum is then freed so as to permit an extensive resection of the tumor. If a sufficiently extensive resection of the tumor cannot be done, to leave at least 4 cm. of healthy tissue below it, amputation of the rectum is indicated. The peritoneum is closed before section of the intestine. The method of terminating the operation depends upon the general condition of the patient, and the extent of the resection. If sufficient intestine remains, immediate end-to-end suture of the colon to the ampulla may be done. In other cases, if the colon is long and most of the rectum has been removed, Hochenegg's technique of invagination of the colon in the anus may be employed. In some cases a sacral anus must be formed, and a continuity of the intestines re-established at a second operation, after a sufficient prolapse of the intestine has occurred, usually in from six to fifteen months. This gives the least satisfactory results, but is sometimes the only method possible.

In some cases a combined abdominosacral method is employed, on the same principle as the combined abdominoperineal method. The abdominal operation is done first, to facilitate the liberation of the pelvic colon. When rectal amputation is indicated the combined perineosacral method is employed. Seventeen cases are reported in which the transsacral route was employed in cancer of the rectum with only 3 postoperative deaths, 1 due to infection and the 2 others to shock. In most cases there was little or no postoperative shock. ALICE M. MEYERS.

LIVER, GALL BLADDER, PANCREAS, AND SPLEEN

Biasini, A.: Occlusion of the Hepatic Artery and of the Common Duct (Occlusioni dell'arteria epatica e del coledoco). *Arch. ital. di chir.*, 1938, 48: 277.

The author states that hepatic function has been the subject of numerous studies during the last few years. In the present investigation, Biasini is primarily interested in the modifications of hepatic function resulting from the ligation of the hepatic artery and of the extrahepatic bile passages.

In surgical practice, ligation of the hepatic artery is most commonly performed for hemostatic purposes in cases of aneurysm and of traumatic lesions of this vessel.

Obstruction of the biliary passages is of more common occurrence in medical practice. It is encountered in biliary calculosis, in certain tumors, cicatricial stenosis, certain parasitic infestations, obstructions of the endocanalicular system, calcification of the internal elastic membrane, and cirrhosis of the liver.

In some pathological cases, the arterial blood supply as well as the biliary passages may be obstructed, as is the case in aneurysm of the hepatic or superior mesenteric artery with pressure upon the bile ducts.

Biasini used only dogs as experimental animals and sub-divided the various groups according to the type of intervention as follows: (1) simple ligation of the hepatic artery; (2) simple ligation of the ductus choledochus; (3) simultaneous ligation of the hepatic artery and the common duct; (4) primary ligation of the hepatic artery and secondary ligation of the common duct; and (5) primary ligation of the common duct followed by secondary ligation of the hepatic artery.

Following the operation, the author studied the effects upon the individual functional components of the liver and he observed also the blood sugar, the non-protein nitrogen level of the blood, the acid-base equilibrium of the blood, and the physico-chemical character of the bile.

Biasini also studied the roentgenological picture of the gall bladder following ligation of the bile ducts. In dogs in which the hepatic artery was ligated, he studied the establishment of an arterial collateral circulation.

From the results obtained, he concludes that ligation of the common hepatic artery is not followed by grave disturbances; compensation follows easily, and the obstruction is not incompatible with life. Contemporaneous ligation of the hepatic artery and of the biliary ducts, on the other hand, is rapidly followed by grave disturbances resulting in the death of the animal.

Variously combined ligations usually result in permanent disturbances which are rarely compatible with life. Simple ligation of the common duct followed by secondary ligation of the hepatic artery seems to be the least dangerous procedure in this respect.

The author then analyzes the results critically and comparatively and brings them into analogy with various human pathological conditions.

He discusses the organofunctional changes resulting from the occlusion of the hepatic artery and of the common duct and emphasizes that occlusion of the hepatic artery, although of a certain gravity, does not cause death of the animal. Occlusion of the common duct, on the other hand, calls for immediate surgical intervention if all the indications are present. RICHARD E. SOMMA, M.D.

Ravdin, I. S., Rhoads, J. E., Frazier, W. D., and Ulin, A. W.: The Effect of Recent Advances in Biliary Physiology on the Mortality Following Operation for Common-Duct Obstruction. *Surgery*, 1938, 3: 805.

In the period between 1922 and 1937, 155 patients with obstructive jaundice were operated upon at the Hospital of the University of Pennsylvania. These cases were analyzed for the effect of a changing pre-operative and postoperative régime on morbidity and mortality. The series was divided into three groups. The differences in pre-operative and postoperative treatment in these groups are summarized in the following table:

VARIATIONS IN PRE-OPERATIVE AND POSTOPERATIVE THERAPY

Group	I	II	III
Years	1922–1929	1929–1933	1933–1937
No. of Patients	59	47	49
High Carbohydrate Diet	o	+	++
Calcium	+	±	o
Supplementary Intravenous Glucose			
Pre-operative	±	+	++
Postoperative	±	+	++
Blood Transfusions			
Pre-operative	o	o	++
Postoperative	±	+	++
Operation during Period of Constant Bilirubinemia	o	+	+
Biliary Decompression	o	±	+
Refeeding Bile	o	+	++

The incidence of "pancreatic asthenia," liver shock, and postoperative hemorrhage, and the mortality due to these complications are tabulated in detail for each group. It appears that pancreatic asthenia and liver shock have been encountered with decreasing frequency. Postoperative hemorrhage, however, remains a common complication of operations upon jaundiced patients, but it has been possible to reduce the degree of the bleeding and the mortality of the complication. The operative mortality in the authors' series has been greatly reduced.

The various problems peculiar to the surgery of obstructive jaundice are discussed and the newer methods of pre-operative and postoperative treatment are evaluated. JOHN H. GARLOCK, M.D.

D'Aunoy, R., Ogden, M. A., and Halpert, B.: Primary Carcinoma of the Biliary System. *Surgery*, 1938, 3: 670.

At necropsy, performed in the cases of 6,050 persons over one year of age, primary carcinoma of the biliary system was found in 40 cases. In 23 of these the condition had been primary in the liver (16 liver-cell and 7 cylindrical-cell carcinomas). In 6 it had been primary in the extrahepatic biliary ducts and

in 11 the condition had occurred primarily in the gall bladder (all cylindrical-cell carcinomas). Eight of the patients had died in the fifth, 11 in the sixth, and 14 in the seventh decade of life. The youngest had been thirteen years and the oldest seventy-seven years of age.

In many instances, in addition to local infiltration or spread of the condition by way of the lymph and blood vessels, metastases had occurred in the regional lymph nodes or in distant organs. Practically all of the patients with primary liver growths had had cirrhosis of the liver with ascites. The majority of patients with primary growths in the extrahepatic ducts and in the gall bladder had had cholelithiasis. With few exceptions, the patients had been jaundiced. The average duration of illness had been four and one-half months.

Earlier reports on neoplasms of the biliary system show that the incidence of primary carcinoma of the liver varies in different geographical locations. Similar variation seems to exist with regard to the site of the primary growth. The authors' series is remarkable in that the primary carcinomas of the liver had a high incidence and far outnumbered the carcinomas which were primary in the extrahepatic biliary ducts and in the gall bladder.

The series is furthermore unusual in that practically all of the patients with primary carcinoma of the liver had cirrhosis of the liver with ascites, irrespective of the histological structure of the growths. Few of them had cholelithiasis, whereas the majority of the patients with primary growths in the extrahepatic biliary ducts and in the gall bladder had cholelithiasis. Jaundice occurred in practically all of the cases, irrespective of the site or the histological type of the primary growth.

JOSEPH K. NARAT, M.D.

Craft, C. B.: The Effect of Ephedrine on Pancreatic Secretion: A Method for the Management of Patients Having a Pancreatic Fistula. *Surgery*, 1938, 4: 64.

The results of animal experimentation clearly indicate that 10 mgm. of ephedrine given subcutaneously decrease the volume output of pancreatic juice. This observation agrees with the action of epinephrine on pancreatic secretion. Like epinephrine, ephedrine probably produces its inhibitory effect on the secretion of pancreatic juice through its vasoconstrictor action on the blood vessels of the pancreas, which results in a decrease in the minute flow of blood to the pancreas and a decrease in secretion of pancreatic juice. Ephedrine begins to exert its vasoconstrictor action about ten to fifteen minutes after injection and continues to exert its effect for the next twenty or thirty minutes.

In the doses used to decrease the secretion of the pancreas, ephedrine produced no toxic manifestations in animals. Ephedrine is a drug which should be tried for the reduction of pancreatic secretion in cases of pancreatic fistula. The amount of ephedrine that would be required to reduce the secretion of the pancreas in man cannot be stated; however, a single dose of 400 mgm., or the administration of 150 mgm. every three or four hours during the day and night has produced no serious results.

Silica gel has proved to be very valuable in the control of the skin excoriation and tissue digestion in two clinical cases. It has been used on the theory that it absorbs enzymes. It is a neutral powder, very soothing, non-irritating, and easily applied.

SAMUEL KAHN, M.D.

Nordmann, O.: Newer Views on Acute Pancreatic Necrosis and Its Treatment (Neuere Anschauungen ueber die akute Pankreasnekrose und ihre Bekaempfung). *62 Tag. d. deutsch. Ges. f. Chir.*, Berlin, 1938.

In view of evidence derived from pathological anatomy and physiology, the term pancreatitis is incorrect and pancreatic necrosis should be substituted, since autodigestion of the gland is important at the outset of pancreatic edema, and even more important in its later stages. The condition is secondary to gall stones or to gall-bladder disease without stone. Stone in the ampulla is much rarer than is usually believed. The mechanical origin of pancreatic necrosis from the entrance of bile into the pancreas is not the chief cause of necroses. If a communication exists between the pancreatic and common bile ducts, pancreatic juice probably passes over into the bile duct because of the higher pressure, where it becomes activated and then, by diffusion or backflow, causes autodigestion of the gland. Much more important than the ductal origin are functional disturbances, altered circulation, stasis, protein decomposition, leucocytic extravasation: in short, circulatory disturbances and fermentative processes. There are gradations from simple edema to total necrosis. Glandular inflammation occurs rarely, usually extending from adjacent organs to the peripancreatic glands, injuring the pancreas, and giving rise to necroses.

In diagnosis, the diastasis test is of primary importance; however it is absolutely positive only on the first to second days; prognostically it is of no value. The outlook is unfavorable only if it remains persistently high. Painstaking technique is a prerequisite for positive results. Lipase determination is as yet not reliable. Leucocyte counts occasionally elevated to as high as 50,000 are considered prognostically unfavorable. Non-protein nitrogen retention and anuria are not due to bacterial poisons but to protein destruction. Marked elevation of the blood sugar is a serious prognostic sign. Shock is due to protein decomposition products; cyanosis to paralysis of the vasomotors. Hematemesis, a bad omen, is due to backflow of the blood from the pancreas into the duodenum and, thence, into the stomach.

Drainage of the peritoneal cavity is of no avail. The exudate is sterile at first. Trypsin is not injurious and fat necrosis is of no significance. Exploratory laparotomy was done in 4 cases, and the

abdomen closed. In spite of massive exudate and innumerable fat necroses, smooth recovery took place. Manipulation of the gland is dangerous as it increases necrosis within the pancreas. Cholecystectomy and drainage of the common duct do not improve the outlook. Such casual therapy should be attempted if the general condition is good and the gall-bladder symptoms are predominant. The pancreas should always remain untouched. The results of all such operations are bad, with a mortality of from 50 to 80 per cent. The changes in the gland progress irresistibly, even with early operation. The fate of the patient is sealed the instant the disease breaks out, and is not to be influenced by operative measures. If the diagnosis is uncertain, exploratory operation should be done, but one should proceed conservatively if pancreatic necrosis is found. The mortality with conservative treatment is, at most, 25 per cent. In one-third of the patients who recover, abscesses subsequently develop in the lesser sac, beneath the diaphragm, or in the pancreas itself. Prophylaxis and the prevention of recurrence consist in early radical operation of the gall-bladder disease. Such disease must be suspected following an attack of pancreatic necrosis, even if the previous history is not definite. If operation is not done, chronic pancreatitis may develop. In patients who recover, alimentary glycosuria must be watched for. Conservative treatment of acute pancreatic necrosis was also recommended by Koerte, in his famous monograph. His return to his original indications seems, in the light of newer investigations, to be in the best interests of the patient.

(NORDMANN). LEO M. ZIMMERMAN, M.D.

Boyce, F. F., and McFetridge, E. M.: An Experimental Study of Operations Which Involve Exclusion of the Pancreatic Secretion from the Intestinal Tract, with Special Reference to the Possible Effects on Protein and Fat Digestion and on the Metabolism of the Liver Cell. *Surgery*, 1938, 4: 51.

The authors report their experiments on animals in which the external pancreatic secretion was excluded from the intestinal tract by various methods.

The digestion of fat and protein was approximately normal in all the animals even when a diet unusually rich in these substances was given. In spite of this fact, however, fatty changes in the liver developed in the animals in which partial or complete pancreatectomy was done. However, if lecithin was added to the diet of these animals fatty changes did not develop in them; neither did fatty changes develop in animals in which the pancreatic ducts were ligated and divided but in which the pancreas was left *in situ*.

The experimental evidence outlined seems to corroborate Dragstedt's assumption of a pancreatic hormone which can take over the function hitherto assigned exclusively to the external secretion.

The clinical application of this experimental work suggests:

1. That radical surgery which does not involve excision of the pancreatic tissue may safely be done, without re-implantation of the pancreatic ducts, for malignancies of the ampullar and periampullar regions. In such cases fatty infiltration of the liver is not likely to develop.

2. That when such surgery must include excision of the head or of the head and body of the pancreas, fatty changes will develop within the liver unless lecithin, choline, pancreatic substance, or alcoholic extracts of the pancreas be administered to forestall them.

SAMUEL KAHN, M.D.

La Barre, J.: Experimental Pancreatectomy (La pancréatectomie expérimentale). *J. internat. de chir.*, 1938, 3: 277.

La Barre states that partial or total removal of the pancreas has been an important operation performed on animals to study the rôle played by this organ in the regulation of the blood sugar and in the elaboration of its digestive enzymes. Partial pancreatectomy has also been found to be a useful operation in certain hypoglycemic states due to the overproduction of insulin by a hyperplastic or neoplastic pancreas.

After having described some of the original methods of depancreatization in the dog, the author briefly reviews the anatomical features of this gland and outlines the methods of its partial or total removal. After the animal has been suitably anesthetized, the abdominal cavity is exposed, the tail of the pancreas is liberated, the gastrosplenic portion is extirpated, and the head is separated from the duodenum, care being taken that the pancreaticoduodenal artery which supplies this portion of the intestine is not injured. Any residual portion of the gland is removed by curettage.

Depancreatized dogs invariably develop diabetes, which is usually combated by the daily administration of from 6 to 8 units of insulin, beginning on the second day after the operation. In order to offset the digestive disturbances resulting from the absence of the pancreatic enzymes, the animal is given 200 gm. of raw pancreas two or three times a week. Concerning the partial removal of the gland, Minkowski has shown that definite symptoms of diabetes appear if one-fifteenth of the total pancreatic tissue is left *in situ*. In general, the degree of severity of the diabetes depends upon the quantity of pancreatic tissue which has been removed.

La Barre furthermore discusses the biochemical changes which follow partial or total pancreatectomy, such as hyperglycemia, glycosuria, acidosis, and uremia. In this connection, the author points out that glycosuria is primarily conditioned by a renal factor and that this symptom, therefore, should never be considered a basis for estimating the severity of the hyperglycemia. He also points out that in diabetes the nitrogen metabolism is profoundly disturbed, as can be observed from the greatly increased nitrogen elimination. This disturbance is most frequently accompanied by acidosis

and severe malnutrition. It is therefore essential to maintain a suitable nitrogen equilibrium, which can be done only by insulinization. The author also describes the surgical interventions on the nerve supply of the pancreas intended for the relief of certain diabetic conditions.

After having discussed the historical features of diabetes mellitus resulting from hyposecretion of the islands of Langerhans, the author describes certain hypoglycemic states resulting from hyperinsulinism. This disorder was first described in 1924 by Harris, who called attention to a clinical condition characterized by extreme weakness, a tendency toward syncope, an intense hunger sensation, and hypoglycemia. Later it was found that this disturbance is primarily due to hyperactivity of the islands of Langerhans resulting from certain neoplastic changes within that tissue. Subtotal pancreatectomy is the operation of choice in this clinical syndrome.

La Barre does not recommend perivascular sympathectomies which certain investigators advocate for the improvement of diabetic conditions.

RICHARD E. SOMMA, M.D.

MISCELLANEOUS

Severi, A.: Experimental Research on Endoperitoneal Bacteriophage Therapy (Ricerche sperimentali sulla batteriofagoterapia endoperitoneale). *Clin. chir.*, 1938, 14: 165.

Severi states that bacteriophage therapy was introduced in Italy as early as 1924 by Alessandrini and Doria in the treatment of typhoid fever. They reported good results in about 50 per cent of the cases. These investigators observed in most cases an attenuated course and a markedly shortened duration of the disease. The bacteriophage was administered orally and intravenously in these cases.

Severi used guinea pigs and rabbits as experimental animals. Into these animals he injected intraperitoneally broth cultures of staphylococcus aureus obtained from cases of osteomyelitis, bacillus coli, paratyphoid A and B, and mixed cultures. A certain number of control animals were allowed to die; another group received an intraperitoneal injection of the specific bacteriophage immediately after the bacterial inoculation. Animals injected with a mixed bacterial broth culture received a specific polyvalent bacteriophage. Into another series of animals the author injected the bacteriophage at various time intervals (up to six hours) following the broth culture inoculation.

Besides observing the general effect of the bacteriophage, the author also studied the speed of microbic absorption from the peritoneal serosa, the behavior of the non-protein nitrogen level in the blood, and the leucocytic curve in relation to the peritoneal infection and to the bacteriophage therapy. Also the thermal elevations and the pulse were recorded.

From the results obtained, the author concludes that the action of bacteriophage introduced into the infected peritoneal cavity is quite noteworthy if the latter is administered contemporaneously with the pathogenic organism (staphylococcus pyogenes aureus, bacillus coli, or paratyphoid B). In order to obtain satisfactory results the bacteriophage must be specific for every type of organism.

The author also found that if the bacteriophage injected into the peritoneal cavity neutralizes the action of the virulent organism, examination of the blood reveals a marked leucocytosis, but the absence of such a finding indicates that the bacteriophage has failed to act.

In the presence of a well acting bacteriophage, the thermoregulatory center is stimulated and there is a marked rise in the temperature; this rise does not occur, however, in control animals or in cases in which the bacteriophage fails to overcome the virulence of the infecting organism.

Furthermore Severi found that following the bacterial inoculation, the non-protein nitrogen level in the blood was slightly raised. This phenomenon occurred in the control animals as well as in animals which were treated with the bacteriophage.

The organisms injected into the peritoneal cavity appeared in the blood stream after five minutes in control animals as well as in those treated with bacteriophage, but in the latter group the blood cultures became negative after twelve hours.

Severi also found that the bacteriophage administered even two hours after the inoculation was capable of neutralizing the action of the infecting organism, but if administered later, its effect rapidly diminished. After four hours the action of the bacteriophage ceased completely.

The author believes that bacteriophage therapy is of unquestionable value, and that this principle should be applied more frequently in human cases.

RICHARD E. SOMMA, M.D.

INFLAMMATION OF THE UPPER URINARY TRACT COMPLICATING THE REPRODUCTIVE PERIOD OF WOMAN

Collective Review

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DURING the course of the past few years extensive experimental and clinical studies have yielded much valuable information in regard to the physiology of urinary elimination in normal pregnant and non-pregnant women, and to the etiological relationship this bears to the inflammatory processes which often complicate the gravid state. In addition, new concepts of the syndrome commonly known as pyelitis of pregnancy have evolved and several advances in treatment have been made.

A critical review of this voluminous work, a large part of which is not readily accessible to the obstetrician, seems desirable for the purpose of familiarizing him with the literature and enabling him to utilize the information it contains. The multiplicity of these reports and investigations has resulted inevitably in some differences of opinion as to the factors responsible for the increased incidence of inflammation of the urinary tract in pregnancy, as well as to the best methods for therapeutic relief. However, it is possible to trace a gradual but definite consolidation of experience, with the result that today we, as clinicians, are more able than ever before to treat the disease effectually.

In making this survey it has been necessary to exercise a considerable degree of discrimination in order that its length might be kept within reasonable limits. For this reason, although the literature has been thoroughly scrutinized, many reports of a confirmatory nature have been deleted. Even so, it has seemed necessary to quote the 330 references cited in the appended bibliography. As will be seen, most of these are in the German, British, American, French, and Italian journals. All have been read in their original form and the significant facts consolidated into this résumé. Extensive reviews attempting the same objective have appeared in the literature of other countries. Those worthy of particular mention are those of Contiades (36–44), Baird (7–11), De Beaufond (65), Hanlo (107), and Bompiani (24).

The title appearing at the head of this review was chosen after much consideration, because there was found to be such a diversity of nomenclature applied to inflammation of the urinary tract in general, and even to the relatively well recognized syndrome encountered in pregnancy, as to make the choice of any of the common appellations not only difficult but certain to lead to misconception.

DEFINITIONS

In an attempt to bring some degree of consistency into the prevailing confusion and inaccuracies of terminology, we shall use a simple anatomicopathological system of nomenclature, not only because it is already in use in some quarters and is readily understood, but also because it is more accurately descriptive and can be applied to the male as well as to the pregnant or non-pregnant female.

Inflammations of the tissues of the urinary bladder will be termed cystitis; those of the ureter, ureteritis; of the renal pelvis, pyelitis; and those of the renal parenchyma, nephritis. Inasmuch as the commonest involvement of the urinary tract in pregnancy, usually called "pyelitis of pregnancy," embraces primarily the renal pelvis and ureter, one may properly, according to this system, term the syndrome pyelo-ureteritis of pregnancy; and when, as sometimes happens, the process extends to the renal parenchyma, one should speak of pyelonephritis or, more accurately, pyelo-ureteronephritis. However, the latter is cumbersome and may be safely contracted to pyelonephritis. Nevertheless, to speak clinically of pyelonephritis of pregnancy as the common complication of pregnancy, as is done frequently in France and sometimes in this country, is misleading because demonstrable involvement of the renal cortex is seen only infrequently. The term in most common use to convey the concept

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of the usual syndrome is "pyelitis of pregnancy." This evokes less criticism but, like others, it is inaccurate in that it does not completely indicate the structures involved in the pathological process. In addition, it indicates that it is peculiar to pregnancy, which is not true, for we have the same disease process in children and in non-pregnant women.

Kamniker (142) writes of "pyelitis gravidarum" and gives the following definition: "an inflammation of the renal pelvis in which, in most instances, the parenchyma is more or less involved; less often, the ureter, and least often, the bladder." This definition has the merit of clarity, but expresses belief in parenchymal involvement of the kidney as a common event, a belief which most observers do not share because the results of such involvement are not clinically demonstrable, either during the febrile phase or later, with rare exceptions.

Wear (317) gives the following definition: "Pyelitis is non-suppurative pyelonephritis," a very confusing statement because the terms used in the definition are themselves indefinite. Other terms frequently found are: "pyelitis collibacillaire" and "pyelocystitis" or "cysto-pyelonephritis gravidique." Enough has been said to indicate not only the variety of terms that have been coined to identify the disease, but also to point out the confusion that exists as to the structures usually involved. It is obvious that a simple, accurate system of nomenclature is urgently needed, hence we propose the one outlined, which uses a simple anatomicopathological basis.

The characteristics of pyelo-ureteritis, its common variations, and complications, together with the structures involved, will be systematically presented. However, inasmuch as many of the variations, as well as the incidence and sequelæ, are dependent upon the altered anatomy and physiology of the urinary tract characteristic of pregnancy, the latter should be considered first.

ANATOMICAL CHANGES IN THE URINARY TRACT

In the non-pregnant woman the urinary bladder lies rather low in the pelvis and its posterior surface is in direct approximation to the uterus and vagina. These latter organs give the base of the bladder its anterior convexity and, at the same time, produce slight depressions at either end of the interureteral ridge in which the ureteral orifices lie. This relationship of the base of the bladder to the uterus and vagina is significant because of the marked changes which pregnancy and parturition produce in the birth canal. Were it not for the loose areolar connective tissue uniting the bladder to the uterus, the former would, of course, be stretched excessively during labor; however, this relationship provides the necessary freedom of movement.

With the advent of pregnancy the texture of the uniting connective tissue becomes even more flexible. The trigone, or that portion of the base of the bladder lying between the ureteral orifices and the internal urethra, is much more intimately adherent to the vagina, so that it does not accommodate itself as adequately as other portions of the bladder to the enlargement of the uterus, and more particularly to the passage of the fetal head, with the result that overstretching, occasional tear of muscular elements, and edema are common in this physiologically important portion of the bladder.

Previous to the fourth month of pregnancy few significant changes take place in the bladder, whereas from the fourth month to term marked alterations occur. With the increase in size of the uterus, the bladder is carried upward so that when distended with urine it leaves the pelvis and becomes an abdominal organ. The generalized hyperemia characteristic of all pelvic organs in pregnancy is shared by the bladder and ureters to such a degree that there is marked increase in the caliber and tortuosity of all blood vessels, particularly toward term.

With the descent of the fetus into the pelvic cavity, the base of the bladder is further curved anteriorly by the pressure of the presenting part, which tends to produce passive congestion and edema of the tissues, which in turn make these tissues increasingly vulnerable to trauma and infection. The existence of these factors, and the close relationship of the trigone to the vagina, explain the background for the common bladder difficulties, such as incontinence, retention of residual urine, inability to void, and cystocele, often seen in the post-partum period.

The upper urinary tract, that is, the ureters, kidney pelves, and calyces, also undergoes an important series of changes characteristic of pregnancy. With the implantation of the ovum, a process of hypertrophy (Kuestner, 158 and Lœffler, 181) is initiated in all these structures, similar to that occurring in the genital tract, whereby, as pregnancy progresses, the walls thicken, particularly in the muscular and areolar connective-tissue portions, so that by term a definite increase is uniformly demonstrable (Hofbauer, 123; Mengert, 199). The ureter, particularly, responds in this way and, in addition, becomes elongated, tortuous, and possessed of a markedly increased lumen, so that it normally

accommodates a greatly increased and, hence, a more static column of urinary fluid. This change in the ureter is seen in over 80 per cent of all pregnant women, and is so striking as to be termed the "physiological hydro-ureter of pregnancy." Baird (10) found dilatation of the tract most common on the right side: 69 per cent in primigravidas, and only 25 per cent in multiparæ; while Kretschmer, Heaney, and Ockuly (156) made the following detailed observations concerning dilatation of the tract in 54 normal pregnant women who were studied radiographically:

TABLE I.—DILATATION OF URETER IN PREGNANCY

FIRST PERIOD: SECOND TO FIFTH MONTHS

	Calyces	Pelvis	Lumbar Ureter	Pelvic Ureter
Percentage on right side.....	52	54	52	1.7
Percentage on left side.....	15	18	35	3.4

SECOND PERIOD: SIXTH TO NINTH MONTHS

	Calyces	Pelvis	Lumbar Ureter	Pelvic Ureter
Percentage on right side...	92	86	74	0
Percentage on left side....	30	30	53.9	0

Somewhat to the contrary, Schumacher (265), who studied 100 normal pregnant women, using intravenous pyelography and stereoscopic technique in the roentgenograms, found little or no change in the first four months; whereas, in the fifth and sixth months there was definite dilatation in the abdominal ureter, measurable in 51 per cent; and in the seventh and eighth months, dilatation was marked in 80 per cent. In addition, he noted a marked lateral displacement of the abdominal ureter and posterior displacement of the pelvic ureter, with no dilatation of the latter at any time.

Usually the normal ureter and kidney pelvis will accommodate from 6 to 15 c.cm. of fluid, but as Crabtree (54) has observed from his measurements, this cubic capacity may be increased from 20 to 60 c.cm. as a result of the changes normally incident to pregnancy. Only 15 per cent of pregnant women, according to the opinion of the majority of observers, may be said not to develop this increased capacity for retaining urinary fluid.

As a result, therefore, of these and many confirmatory studies, we know that the upper urinary tract, that is, the ureter from the pelvic brim upward, together with the renal pelvis and the calyces, undergoes a process of hypertrophy and dilatation in the majority of normally pregnant women, and that this change is much more frequent and more marked upon the right side than it is upon the left; and, furthermore, that no similar alteration is seen in the pelvic portion of the ureter below the lower extremity of the psoas muscle. This increased size is associated with an increase in the fluid-containing capacity, of from two to six times the capacity observed in the tract of the normal non-gravid woman. In other words, there is a partial stagnation of urine or a physiological hydro-ureter.

The reason for the greater dilatation upon the right side as compared to the left seems best explained upon a mechanical basis. Bachrach (6), Francke (87), and Heckenbach (112), as well as Baird (11) and others, have shown that pelvic tumors, tumors of the liver, gall bladder, and pancreas, and pelvic inflammatory disease can, by the pressure they exert upon the ureter, bring about a certain degree of unilateral ureteral dilatation in some ways similar to that seen in pregnancy, the dilatation disappearing when these abnormalities are satisfactorily removed. Many have thought the fetal presenting part was responsible for the mechanical obstruction; however, this thesis has been effectively disproved. Halban seems to have been the first who suggested that the common dextro-rotation of the uterus provided more complete occlusion of the right ureter than of the left, and that this, at least in part, accounted for the more frequent and more marked enlargement upon the right side. Others, Baker and Lewis (12), have emphasized the protective influence of the sigmoid colon at the pelvic brim on the left as being effective in preventing the pressure of the enlarged uterus upon the left ureteral tract. The consensus of opinion seems to be that the pressure of the pregnant uterus together with its dextro-torsion are the mechanical factors which tend to cause dilatation of the ureters above the pelvic brim. However, it is also accepted that there are additional influences at work; otherwise one cannot explain dilatation commencing at the fourth month when the uterus is too small to obturate the pelvic inlet, on the one hand, and, on the other, the mechanical pressure theory does not explain the confirmed observation that the ureters decrease in size during the last month of pregnancy when, presumably, the uterus because of its size is capable of exerting its greatest occlusive effect. This additional factor is to be explained by a consideration of the physiological variations of the ureter and kidney pelvis in pregnancy.

THE PHYSIOLOGY OF THE UPPER URINARY TRACT

Whereas the physiology of the renal cortex and that of the bladder have received a vast amount

of study in the past, the tract between the foramina papillaria and the ureterovesical valves has only recently had intensive study devoted to it. The intrinsic motility of smooth muscle in general is well known, and as the renal calyces and pelves and the ureters are supplied with coats of smooth muscle, the tract was from the first supposed to be possessed of peristaltic activity. DuBois-Reymond (80) was one of the earlier investigators who studied the mode of urine propulsion by the ureter, and as a result of his studies came to the conclusion that the origin of the contractile impulse was at the ureteropelvic junction, or possibly in the renal pelvis itself. Jona (139), Fuchs (93), and others have confirmed the principle that in the musculature of the kidney pelvis lies the pacemaker for the peristaltic activity of the tract. Jona (139) has very clearly shown the systematic and propulsive action of contractions of the renal calyces which force urine into the pelvis of the kidney and are then followed by contraction of the pelvic musculature, while the calyces are still in systole, the combined effect of which is to force urine into the relaxed upper portion of the ureter. Fuchs (93) has studied the ureteral action and describes the formation of cystoids in the ureter, which receive urine from above and then force it onward by a detrusor action of the ureteral musculature. Three principal zones for this type of cystoid-detrusor activity are described by Fuchs: two in the abdominal spindle of the ureter, and one in the pelvic portion. DuBois-Reymond (80) has also theorized as to the nature of the stimulus which incites contraction, and postulated three possibilities: (1) true mechanical stimuli such as would be provided by the bulk of the secreted urine; (2) the agency of the autonomic nervous system; and (3) a hormonic impulse. He concluded that the secretory pressure of the kidney could easily provide the mechanical stimulus, and came to the conclusion that this was most probably the correct explanation.

In short, the renal calyces, the renal pelvis, and the ureter have been shown to constitute a type of pump which forces the products of the kidney into the urinary bladder for storage.

This mechanism for building up pressure is a most necessary one, for it has been demonstrated by Kreutzmann (157) and Wuellenweber (327, 328) that fluid pressures are normally higher in the semi-filled bladder than in the renal pelvis, that the kidney is not, therefore, drained by gravity, and that the pelvi-ureteral musculature is a necessary provision for evacuation of the chambers of the kidney. The average pressure in the renal pelvis is 80 mm. of water, whereas the average pressure in the partially filled bladder is 90 mm. of water in the non-pregnant female, which findings indicate that there is a constant head of pressure in the bladder against which the ureter must work.

Creevy (59) has very ably summarized the evidence concerning intrapelvic, intra-ureteral and intracystic urinary pressures in the normal non-gravid individual, and states that the intravesical tension is uniformly higher than the pressure in the renal pelvis, and that the greater pressures attained in the bladder and lower ureter are the result of the forces exerted by the renal pelvis and ureter combined. This relationship requires some provision to protect the kidney against these pressures. A fourfold mechanism exists for this purpose: (1) the ureterovesical valve; (2) the oblique course of the ureter through the bladder wall; (3) the peristaltic activity of the ureter (this being the most important of all, for Creevy has demonstrated that a short segment of the ureter is capable of exerting a pressure of 90 mm. of water); and (4) an autonomic bladder reflex which stops ureteral peristalsis during periods of sudden intravesical tension (Boeminghaus, 21).

Further, Kreutzmann (157) and Wuellenweber (328) have established that during pregnancy not only is this pressure relationship reversed, but that considerably higher pressures are the rule in the renal pelvis; thus they found the average intrapelvic pressure during pregnancy to be 240 mm. of water, whereas that in the urinary bladder falls to an average of 70 mm. of water. Logically they conclude that the pelvi-ureteral pump is decompensated by some factor characteristic of pregnancy, and that to a great extent urinary evacuation in the tract becomes a function of higher pressures resulting from the secretory activity of the renal parenchyma. As DuBois-Reymond (80) and Andler (3) have shown the kidney to be capable of exerting secretory pressures on the average of 50 mm. of mercury or 680 mm. of water, this is a very possible function for the kidney to assume. In other words, it is supposed that the kidney cortex, by virtue of its secretory pressures, forces urine through the atonic urinary tract into the bladder where it is stored.

However, these elevated pressures are associated in all probability with side-effects. It seems likely that the dilatation of the kidney pelvis and ureter may be an expression of them, on the one hand and, on the other, since it is well known that increased secretory pressures in the kidney are only possible as a result of an elevation in blood pressure, it may well be that decompensa-

tion of the musculature of the urinary tract is the explanation of some of the hypertensive phenomena of pregnancy. This latter possibility has been suggested by Hayes (110), Baird (8), Eufinger (83), and others.

URETERAL ATONY IN PREGNANCY

For nearly a hundred years it has been known that dilatation of the ureteral tracts is common in pregnancy, but not until the past twenty-five years has it been realized that mechanical obstacles, such as the enlarged uterus and torsion, did not suffice to account for this phenomenon. Stoeckel (288), Weibel (318), and Kaltenschnee (141) all realized that an atony of the musculature must also exist. These and various other reporters assigned bacterial toxins, overdistention of the musculature, changes in the calcium and potassium ions in the urine, altered neuromuscular mechanism, and a variety of other factors as the causes of the atony.

That atony did exist was strongly suggested by the work of Kaltenschnee (141), Gremme (101), Pflaumer (227), Baird (8), Bolhuis (23), Mandruzzato (189), Paladini (215), Rao (242), Seitz (271), Sellheim (272), and Sorrentino (279), to name only a few. However, the proof of its existence and incidence in relation to the various months of pregnancy, as well as its exact relationship to dilatation of the ureter, was not available until recently when Traut and McLane (302) showed conclusively that dilatation of the tract as measured by pyelograms is inversely proportional to the degree of atony as expressed by kymographic tracings. We now know that the decompensation of the pyelo-ureteral mechanism is due to an altered irritability of the musculature and that it is a concomitant of normal pregnancy.

Much work has been done to explain why the ureteral musculature should undergo these atonic phases. Lœffler (181), in an attempt to explain all on a mechanical basis, postulated first an increasing degree of obstruction to the ureter due to the increasing size of the uterus. This obstruction, he thought, causes the ureter to undergo hypertrophy of its muscular elements in an attempt to compensate for the increased effort necessary to evacuate the tract. Ultimately, in the majority of women, he argued, this period of compensation passes into one of decompensation with associated dilatation of the ureter and kidney pelvis, and is associated inevitably with atrophy of the musculature and stagnation of the urinary stream.

That this explanation cannot be adequate has been apparent to many workers, for as Traut and McLane (302) proved, and many others had previously intimated, the ureteral musculature re-establishes intrinsic muscular activity on an increasing scale from the seventh month of pregnancy onward to term, which would seem wholly impossible were not other factors than simple mechanical obstruction at work.

The parallelism between the atony of the ureteral musculature and that inherent in the uterus impressed many observers. Inasmuch as the uterine atony was thought to be due primarily to hormonal influences, it seemed logical to suppose that the atony of the ureter might also be due to chemical influences characteristic of pregnancy. Kidd, in 1920, was probably the first to actually enunciate this idea (Burrows, 27). Hofbauer (122), realizing that a number of smooth muscular structures, such as the colon and gall bladder, were known to be sluggish in their activity in pregnancy, studied the problem from the point of view of the possible influence of increased bile salts. By studying segments of ureter *in vitro*, he felt that he established the observation that increased bile acids circulating in the media of his experiment brought about a decrease in muscular contractibility of the organ.

Bompiani (24), studying the action of the so-called "pregnancy hormones" upon the isolated ureter kept alive *in vitro*, came to other rather startling conclusions. He felt that undoubtedly the urine of the pregnant woman contains substances capable of altering the functional activity of the isolated ureter kept alive *in vitro*, and that this action can be explained only by the effect of these substances upon the circular and longitudinal fibers of the ureter. He found that they altered the energy, rhythm of contractions, and the tone, and so modified the peristalsis or coordinated expression of these factors. The action of these substances eliminated through the renal cortex of the pregnant woman was supposed to affect the motility of the ureter by activating it in the early months and then inhibiting it during the second half of pregnancy. Furthermore, in a series of brilliant experiments Bompiani was able to demonstrate that these inhibitory effects were obtained most markedly by the use of corpus-luteum extracts and least markedly from follicular liquid obtained directly from follicular cysts of the ovary.

Contiades (36–40), using a similar technique, showed that the ureter *in vitro* was rendered much less active by folliculin, corpus-luteum extract, and amniotic fluid, as well as that the untreated urine of pregnant women in the sixth and seventh months definitely depressed the muscular activity

of the ureter. Other workers, particularly Villaret (312, 313), Grossv-Streja (104), and Rossi (252), have performed experiments of various sorts, all tending toward the same conclusions. Philipp (229) has shown that he can bring about dilatation of the non-pregnant woman's ureters very promptly by giving the woman a transfusion with blood from a pregnant donor. He cites his experience in this regard as proof of the hormonal nature of the reactive substance, and states as his belief that the hormones originate in the placenta.

Thus, we have arrived at the conclusion that the physiological propulsion of urine by the urinary tract is very markedly altered during pregnancy, sometimes to the point of complete decompensation; and also that the factors responsible for this alteration are principally chemical in nature, in all probability those essential or intimately concerned with the successful outcome of the gestational function of woman. That mechanical factors, such as torsion of the uterus and pressure of the enlarged uterus upon the tracts, also play a part, no one can doubt; however, the underlying atony seems, in the light of present information, to be the most fundamental cause.

PYELO-URETERITIS

As we have seen, urinary stasis of greater or lesser degree is the usual accompaniment of pregnancy. Therefore, the relatively higher incidence of upper urinary-tract infection in pregnant women than in any other clinical group, excepting perhaps young female children, is easily understood, for the only additional factor necessary to produce the disease syndrome, pyelo-ureteritis, is the introduction of considerable numbers of colon organisms into the upper portions of the tract (Kamniker, 146).

MICRO-ORGANISMS CAUSING INFECTION

All observers agree that bacilli of the colon group of organisms are the chief pathogenic agents producing the inflammatory lesions of the upper urinary tract (80 per cent, Kehrer, 147), although Cathala (31), in 1904, pointed out that the colon organisms having produced an inflammation might, and occasionally did, prepare the way for the other organisms, or secondary invaders, to enter the field, and that when this occurred, the mixed infection resulting not only was more resistant to treatment but also was more apt to develop serious complications.

An analysis of the investigative work along bacteriological lines is fraught with many difficulties because of the different technical methods used, on the one hand (Hundley, 130), and, on the other, because many observers use the total number of positive cultures obtained in reporting their results instead of differentiating between pathogens and non-pathogens, as well as fail to exclude obvious contaminants such as those which are found normally to inhabit the skin surfaces. There are, therefore, wide discrepancies between the findings of different workers.

A statement which is often made is to the effect that the normal kidney can excrete micro-organisms with no impairment to itself or the other urinary organs, and that this so frequently occurs in the pregnant woman that there is a high incidence of bacteriuria (De Beaufond, 67). The earlier observers, such as Albeck (1), and Duncan and Seng (82), found micro-organisms in 50 per cent and 11 per cent, respectively, in the upper urinary tract of normal pregnant women. Such a finding would tend to verify the point of view as given above. However, more recently, McLane and Traut (198), using very careful technique and relatively large quantities of inoculum, recovered only 0.86 per cent of pathogenic bacteria (coliform organisms) from the ureteral urine and 12.0 per cent of all forms of micro-organisms in a group of 30 normal pregnant women, whom they followed with repeated catheterizations throughout pregnancy. Hundley, Siegel, Hatchel, and Dumler (130), using much the same technique with a group of 50 normal pregnant women, also found a low incidence, they obtained positive cultures for coliform organisms from the upper tract in 6 per cent, and from the bladder urine in 9 per cent. This would tend to show that the older view is not necessarily correct and that when a high incidence of the coliform organisms is found, there is in all probability some pathological condition present in the tract, or the organisms are being excreted by the kidney because of abnormalities in other organs, most probably the intestine, as has been emphasized by Kretschmer (153).

The only recent study of bladder urine in which the different types of coliform bacilli were differentiated as to incidence is that of Harris and Herrmann (108), in which they found the following distribution in normal women:

TABLE II.—TYPES OF COLIFORM BACILLI

	Antepartum Per cent	Postpartum Per cent
Escherichia coli	6	5.3
Escherichia communior	2.7	6.0
Alcaligenes fecalis	4.0	3.3
Proteus	0	0
Staphylococcus albus	8	13.3

It is safe to say that the majority of normal pregnant women *may* excrete small numbers of

coliform organisms during pregnancy, and a small percentage may excrete them in fairly large numbers when there is some abnormality which permits their escape from the bowel into the tissue spaces of the body; therefore the evacuation of organisms is accomplished without the accompaniment of any demonstrable inflammatory reaction. This is hard to accept without reservations. It would seem that there *must* be some observable response to a potentially pathogenic organism such as the bacillus coli when it reaches the lymph, blood, or tissue spaces, even though in small numbers. However, if there is a reaction, it is undetectable clinically, so that from the clinical point of view, the first statement must hold until further data are available.

The factors that determine which patient is to develop the inflammatory reaction are only partially known. Dresel has shown that those who respond to the invasion by developing the clinical syndrome of pyelo-ureteritis have an opsonic index which is uniformly lower than that observed in the control groups.

Although stasis of urine in the dilated ureter and kidney pelvis is generally conceded to be the greatest single factor, no one has shown a definite correlation between the severity of the clinical manifestation and the degree of stasis in the urinary tract. On the contrary, some of the severest infections show only slight stasis, and the converse is also occasionally true; however, one rarely sees a pregnant patient with definite clinical pyelo-ureteritis and no demonstrable dilatation of the tract (Kamniker, 145).

Thus far, the only study which has been reported in which a systematic attempt has been made to correlate the clinical picture with the type of organism involved is that of Baird (7). It is well known that there are marked differences in the pathogenicity of the various members of the colon family, so that information of this sort is needed. Baird's findings are as follows:

TABLE III.—TYPE OF INFECTING ORGANISM

Severity of Illness:	1 Per cent	2 Per cent	3 Per cent	4 Per cent	5 Per cent	6 Per cent
Very acute..	10–29	9–25	7–20	8–42	2–14	1–10
Moderate...	16	12	8	7	4	5
Slight.....	8	15	20	4	8	4

1. Bacillus coli communior
2. Bacillus acidi lactici
3. Bacillus coli communis
4. Bacillus aerogenes
5. Bacillus coli anaerogenes
6. Paracolon group

Bacillus proteus is known to be a difficult organism to eradicate by any form of treatment as it requires an acid urine because of its ability to split urea into ammonia, which tends to alkalinize the urine (Lyon, 185). As stated before, it is recognized that when the inflammation is complicated by "secondary invaders" the course of the disease is more complex. Yet no one has thus far indicated what these "secondary invaders" are, excepting that they are usually streptococci, to say nothing of proposing logical means for combating them.

There is, therefore, urgent need for more specific bacteriological study of the micro-organisms in relation to the clinical forms of the disease.

MODE BY WHICH MICRO-ORGANISMS INVADE THE URINARY TRACT

There is marked divergence of opinion as to the route by which micro-organisms reach the kidney pelvis. However, there is general agreement that access must be attained by one of three ways: (1) reflux from the bladder into the ureter and thence by antiperistalsis to the kidney pelvis; (2) by means of the blood stream, being excreted through the glomerular tuft of vessels into the capsule of Bowman and then washed in the urine through the proximal convolutions, loop of Henle, the distal convolutions, and, finally, the collecting duct to the foramen papillarium; and (3) by means of the lymph stream from the ascending colon to the capsule of the right kidney, then by way of the deep lymphatics of the capsule into the parenchyma, or by means of the lymphatics from the vagina and cervix, urethra and bladder, upward along the course of the ureter into the renal pelvis as well as the thoracic duct.

The oldest and simplest view is that involving reflux and antiperistalsis. Antiperistalsis has been shown by Wislocki and O'Connor (324) to occur in experimental animals, while Jona (137) and Trattner (294) have shown that it can occur under certain abnormal conditions in the human ureter. On the other hand, the consensus of opinion, which has grown very weighty, indicates that reflux never occurs normally in the human being, and is seen only under very special pathological conditions.

Blum (18) goes so far as to state that, in the human being, ureterovesical reflux can occur only under the following conditions:

1. In normal ureters and bladders
   - a. In childhood
   - b. Under narcosis
   - c. During ureteral catheterization
   - d. Following nephrectomy
2. In the presence of injured ureterovesical valves
   - a. When there is pathological enlargement of the ureteral ostium

b. Marked infection and infiltration of the ostium
c. In neoplasmic infiltrations of the orifice
d. Sometimes in spinal diseases

3. In some congenital defects
   a. Defects of the ureteral wall
   b. Congenital atony
   c. Megalo-ureter

Schumacher (267) attempted to demonstrate reflux in 100 normal and "pyelitic" women, and was unable to prove a single instance. Bumpus demonstrated only 89 instances of reflux in 1,036 cystograms, and concluded that reflux was never found in the normal bladder except in children. Morris and Brunton (210) examined 104 pregnant women in the last trimester of pregnancy and demonstrated it upon 2 occasions. Frommolt (90) studied many women, some of whom were normal, others with toxemia, and many with pyelo-ureteritis, and was unable to demonstrate the slightest reflux. On the other hand, Gripekoven (103) states dogmatically, but without adequate proof, that "reflux may be produced frequently in pregnancy when the urinary tract is normal."

Legueu and Fisch (169), Sennewald (275), Mikulicz-Radecki (203), and Devraigne and Petit (74), to name only a few, support the hematogenous theory of the origin of the disease. These writers represent the weight of opinion which is based chiefly upon clinical evidence and theoretical considerations. Against their point of view one must place the common experience of all who have made cultures from the blood of patients suffering from pyelo-ureteritis, which indicates that it is extremely rare, even in the height of a chill, that one is able to recover any type of micro-organism from the circulating blood (Devraigne and Petit, 74). In addition, Helmholz (114) has demonstrated in rabbits that when colon bacilli in massive dosage are injected into the vein, suppurative lesions localized in the kidney substance, the papilla, and the adjacent lining of the renal pelvis are the result; whereas, when the organisms are injected without trauma into the bladder, peripelvic and peri-ureteral inflammation result. Helmholz's experiments would seem to indicate that the vascular route is relatively rare in human subjects, because demonstrable cortical lesions in pyelo-ureteritis are rare and are seen only occasionally in patients who have developed pyelonephritis following pyelo-ureteritis.

In short, the assumption that the infection in pyelo-ureteritis of pregnancy usually travels by way of the blood stream is unsupportable because the distribution of pathological lesions is not that which would occur were this the common means of dissemination of the colon organisms.

Weibel (318), Grandjean (100), Walther (316), Holmes (127), Kincaid (149), and Gibberd (97) are among those who choose to interpret their observations of the pyelo-ureteritis syndrome as being the result of the lymphatic spread of micro-organisms. They point out that it can explain: (a) the "ascending type" of infection from the birth canal, bladder, and urethra; (b) the descending type, probably originating from the bowel, as well as, (c) the occasional invasion of the blood stream because of the relationship of the thoracic duct to the large veins. Furthermore, the distribution of the inflammatory lesions seems to be consistent with this means of dissemination. The experimental proof of the theory is not conclusive, however, and consists principally of the demonstration of lymphatic pathways which could afford access to foci consistent with the pathological observations. Francke (86) demonstrated the relationship of lymphatics passing from the ascending colon to the capsule of the right kidney, while Stahr has shown that lymphatics of the capsule communicate with deep lymph channels of the kidney. Winsbury-White (323) has outlined the relationship of the lymphatic drainage of the pelvic organs to those of the upper ureter, kidney, and thoracic duct. Theoretically, these two general routes can explain both the ascending and descending types of infection, as well as involvement of the blood stream. In the present state of our information, the lymphogenous theory, therefore, seems the most satisfactory one.

RELATIONSHIP OF INTESTINAL STASIS

Many writers have been impressed with the coexistence of intestinal stasis and pyelo-ureteritis. Sellheim (272) points out that normal pregnancy is associated with a loss of tonus in nearly all smooth muscle structures, and many others have called attention to the relative obstipation of the intestine and, particularly, the large bowel. Among those who believe that this may have an important etiological bearing upon inflammatory states of the upper urinary tract we should mention Kretschmer (153), LeLorier (171), Philipp (229), Schickele (259), Sennewald (275), Stoeckel (286), and Vignes (311). It is thought that perhaps stasis of the bowel may promote the passage of colon organisms into the lymphatics or the blood stream, and from there these organisms are transferred to the urinary tract.

RELATIONSHIP OF PREVIOUS URINARY INFECTIONS IN CHILDHOOD, IN THE ADULT, AND FOLLOWING MASTURBATION, COHABITATION, AND DEFLORATION

Helmholz and other pediatricians have suggested that pyelitis in childhood may remain latent over long periods of time to recur in adult life (Lepoutre, 175). Wharton, Gray, and Guild (320) recently studied a group of 30 women who had suffered from well established pyelitis during childhood. They found that 57 per cent, investigated as adults, showed definite stigmas of the previous infection, and that, of these, 11 had experienced recurrent attacks, while 6 still had positive urine cultures for the bacillus coli. Only 1 of the 30 women had developed pyelo-ureteritis of pregnancy; however, only 3 of them had become pregnant. These authors thought that their study did not furnish concrete evidence as to the importance of childhood pyelitis as an etiological factor in pyelitis of pregnancy. It probably does suggest, however, that with the persistent bacilluria, the stasis concomitant to pregnancy would, as the group of patients grows older, produce a much greater incidence of pyelitis in pregnancy.

Freudenberg (88) reports from the Kiel Frauenklinik that 10.1 per cent of their patients with pyelitis had had the disease previous to pregnancy. Petit (226) makes an analogous statement, while Crabtree (56), Prather (234), and Pugh (241) make the observation that previous pyelo-ureteritis, whether incurred in childhood or adult life, predisposes toward a recurrence in pregnancy. Stoeckel (288) calls attention to the fact that many patients acquire pyelitis through small traumatic mucosal tears associated with the acts of masturbation, defloration, and cohabitation. Seitz (271) points out that previous infections of the upper tract, however acquired, make for a poorer prognosis in subsequent attacks.

DIET

Diet as an accessory factor in the development of pyelo-ureteritis of pregnancy has never received more than superficial consideration. As far as can be learned no scientific work has been done upon the subject. Philipp (229), however, is of the opinion that a high protein diet may be more conducive to the occurrence of the disease than one in which fruits and vegetables have a suitable part. Schickele (259) believes that a diet which tends to ward off obstipation is of great importance in prophylaxis, while Vignes (311) states that salt should be plentiful in the diet as hypochlorhydria is a causative factor, and Berge (15) stresses the importance of vitamins, particularly A and D, and a diet which produces an alkaline urine, such as citrus fruits.

TRAUMA

Injury to the urethra, bladder, vagina, and cervix probably are only very occasionally concerned in the production of inflammatory states in the upper ureter and kidney pelvis, excepting in the puerperium. Prather (231) reports a high incidence of post-partum pyelo-ureteritis in a group of patients who had some injury to the bladder during delivery. These bladders all contained much residual urine demanding evacuation, which was accomplished by repeated catheterization of the bladder. In an analogous group in which the post-partum bladder retention was controlled by use of a retention catheter, no patient developed pyelo-ureteritis. Prather (231) and Kincaid (149) believe that the repeated trauma of urethral catheterization was responsible for the transmission of the bacteria to the upper tract. Rose (249) makes a plea for continuous bladder drainage instead of intermittent catheterization for similar reasons. Scott studied the so-called "catheter fever" by taking blood cultures from patients recently catheterized, and concluded that trauma of the urethra is sufficient to produce a transitory coliform bacillemia. The work of Walther and Willoughby (316) also points very strongly to the possibility of lymphatic extension from the posterior urethra to the kidney pelvis in post-partum infections. These authors also believe that extension from the cervix as an aftermath of trauma during delivery should be considered as a source of infection, since they find that 75 per cent of parturient women have endocervicitis.

INCIDENCE OF PYELO-URETERITIS

Authorities vary widely in the figures which they quote concerning the incidence of pyelo-ureteritis. Baird (7) places the incidence at the Glasgow Royal Infirmary at 14 per cent, which is the highest figure to be found in current literature; while at University College Hospital in London, Dodds (75) found only 1.1 per cent afflicted with the disease. The following table gives the data available at the present time:

TABLE IV.—THE INCIDENCE OF PYELO-URETERITIS

	Per cent
Kiel Frauenklinik (Freudenberg)	1.8
Boston Lying-In Hospital (Crabtree)	2.1
New York Lying-In Hospital (Traut)	2.2
London, Guys Hospital (Gibberd)	1 to 2.0
London, University College Hospital (Dodds)	1.1

Glasgow Royal Infirmary (Baird)	14 to 16.0
New York (Pugh)	10.0
San Francisco (Emge)	7.0
Greifswald (Philipp)	3.5
Montreal (Seng)	3.0
Vienna (Latzko) (Lepoutre)	7.0
Amsterdam (Van Rooy)	0.8

Antepartum infections are much more common than puerperal infections. Philipp (229) found only 5.8 per cent occurring in the puerperium, Prather (234), 0.4 per cent; Freudenberg (88), 11 per cent; and Dodds (75), 32 per cent.

In the antenatal period, the second semester is the period of predilection for the onset of an initial attack. Pyelo-ureteritis occurring in the first few months of pregnancy is usually the sequel of an earlier infection.

Freudenberg (88), as well as Duncan and Seng (81), found that multiparity predisposed toward a higher incidence of the disease, while Lepoutre (175), Kretschmer (153), and most of the other writers agreed that if the increased number of pregnancies in multiparas, and hence the increased opportunities for the development of the infection, be taken into account, it will be found that the chances of infection are much greater in primigravidas than in multigravidas.

The great majority of infections are unilateral and occur on the right side. Freudenberg's (88) statistics may be taken as typical. He reports 39 per cent right-sided infections, 9.2 per cent left-sided, and 52 per cent bilateral.

DIAGNOSIS OF PYELO-URETERITIS AND ITS COMPLICATIONS

In the writings upon pyelo-ureteritis complicating pregnancy too much emphasis has quite naturally been placed upon the acute or febrile phase of the disease, because it is so much more obvious and can be diagnosed frequently without the aid of laboratory or other special procedures, with the result that the chronic or afebrile phase has been neglected. Not only this, but the term "pyelitis of pregnancy" has come to mean to most clinicians only the acute phase, with the natural result that they are inclined to consider the patient cured when she becomes afebrile, and realize little or nothing concerning the chronic aspects of the disease. More must be known of the chronic phase (Guéniot, 105), which is more difficult of diagnosis, if further progress is to be made in treating the disease in pregnancy.

The difficulties which surround the diagnosis of infections of the upper urinary tract, particularly those complicating pregnancy, can only be clarified by the use of the cystoscope, the ureteral catheter, and bacteriological studies of urine secured by these means (Philipp, 229). The bacterial content of bladder urine may be most misleading, particularly in the pregnant woman, even though the urine specimen be obtained by catheterization of the bladder (Harris and Herrmann, 108). The diagnosis can be clinched only by studies made upon the ureteral urine. Here, clumped pus cells and the demonstration of bacteria in the urinary sediment, plus cultural methods showing pathogenic organisms, particularly of the colon family, indicate infection and inflammation. If, in addition, the clinical picture of pyelo-ureteritis, namely, hectic fever, tenderness in the costovertebral angle, nausea or vomiting, and anemia, be observed, one has the complete picture of the febrile phase of the disease. However, the afebrile phases, which are even more common, are surrounded with such difficulties that only by urological methods can one arrive at the diagnosis. According to Crabtree and most other students of the disease, it is *seldom possible to cure the patient of the infection during pregnancy*. The most that can be accomplished is to keep it quiescent and the patient afebrile, unless the newer antiseptics, such as sulfanilamide, lend the much needed aid. For the present, the statement should stand as written. This is an important concept, for it usually means that the pathological processes, that is, fibrosis and inflammation, continue until after the uterus is emptied and adequate drainage and the normal motility of the tract are established.

It is, therefore, necessary not only to make a diagnosis but also to evaluate the extent of the processes and their character. The stigma of previous attacks of pyelo-ureteritis should lead one to expect greater difficulty in treating a patient in a recurrent attack during pregnancy, and definitely offers a less optimistic prognosis as to the outcome. Hence, it is important that differential kidney function tests be made so that, if renal excretion be low because of previous disease, one can know which kidney is most compromised and to what extent. A test of the kidney function by means of the intravenous pyelogram, as advocated by Schumacher (268), has proved of great value in pregnancy, for delayed excretion of the opaque substance is usually due to kidney damage. Further, the pyelogram is also of value in yielding information as to deformities of the tract.

If the inflammatory process is unilateral with good kidney excretion on the opposite side, the prognosis is good and the patient may be treated palliatively. On the other hand, if the infection is

bilateral, the outlook is much more sinister, particularly if the patient be some weeks from term.

If the renal cortices are involved in the inflammatory process to such an extent that there is retention of non-protein-nitrogen substances in the blood of from 50 to 65 mgm. per 100 c.cm. of blood, the prognosis is grave (Mikulicz-Radecki, 204; Philipp, 229). Higher levels of nitrogen retention are associated with an almost absolutely bad outcome to both mother and infant. It is, therefore, necessary, as part of the diagnostic procedure, to examine the blood chemically and to repeat this procedure from time to time during the febrile phase of the disease, as this is the only reliable index as to parenchymal involvement.

Mixed infections in which the colon bacillus and some secondary invader are involved are discouraging, as Cathala (31) first demonstrated. Seitz (271) and others have recently emphasized that these infections are more resistant to treatment and the ultimate outcome is apt to be disappointing.

Pyelonephritis, that is, extension of the inflammation into the cortex of the kidney, is one of the most serious complications of the acute phase, although it can also be an outcome of the chronic stage in rare instances. In the mildest form, it amounts only to a localized inflammatory edema which closes off the collecting ducts and produces oliguria and nitrogenous retention. In the more severe suppurative types the foregoing results are found, but in addition, bacteriemia, extension to the capsule with the formation of perinephritic abscesses, and ultimately extension to the peritoneum are seen. The outcome of the severer types of complication is usually fatal.

Dozsa (77) has indicated the incidence of pyelonephritis complicating pyelitis as 15 per cent. To other workers this seems somewhat high. Traut (298) reports an incidence of 11 per cent; furthermore, he experienced a maternal mortality of 25 per cent among cases developing this complication. One of the patients did not develop an acute febrile phase at any stage of the disease.

Dozsa (77) first, and others—Fruhinholz (92), Lepage (174), Mayer (197), Paquet (218), and Vignes (311)—since, have called attention to a much rarer complication which simulates acute yellow atrophy in many respects. This they refer to as the "toxic type." In this disease the kidney pain and fever are not so marked and may be negligible. There are marked icterus and liver enlargement, anemia, intractable vomiting, and diarrhea, as well as a rapid pulse, dry tongue, and marked weakness, and sometimes ascites.

According to Preiss (238) there are over 250 cases reported in the literature in which ileus was a complication of pyelo-ureteritis of pregnancy. This author summarizes the different theories concerning the etiological relationship of the two entities, ileus and pyelitis. Stoeckel (286) has given the most logical explanation. He believes that both have a similar background in that normal pregnancy, by means of its hormonal mechanism, produces atony of the ureter as well as atony of the bowel. It produces the "sleeping ureter" with stasis, dilatation, and, sometimes, pyelitis as a sequel, on the one hand, and obstipation of the bowel, on the other, and Stoeckel believes that the latter is merely a minor degree of development of what one sees in ileus. He, therefore, believes that they have a common cause and that it is somewhat remarkable that ileus is not more commonly encountered. The treatment before term is laparotomy because adhesions or a volvulus might be the cause, and these can bring about gangrene. At term, the uterus should be emptied promptly and then, if the ileus remains intractable, laparotomy is indicated for the reasons given above. Other recent writers on this subject are Sennewald (275), Klein (152), Hilgenberg (120), Hellendall (113), and Seitz (271).

EFFECTS OF PYELO-URETERITIS ON THE MOTHER

The immediate effect of infection of the upper urinary tract is, of course, the production of varying degrees of fibrosis of the ureter and renal pelvis, the extent depending upon the duration of the infection, the number of recurrent attacks, and the type of infective agent, for it has been shown that some micro-organisms induce a much greater fibroblastic response than others. The fibrosis may be so slight as only to retard the recovery of ureteral peristalsis following delivery. On the other hand, it may, and too frequently does, produce such an extensive infiltration of scar tissue as to leave the tract devoid of any intrinsic motility. If the scarring is localized, the result may be permanent strictures with hydroureter and hydronephrosis above the point of constriction. Often there is prolonged kidney infection with stone formation, according to Dozsa (78) and Jacobi (134).

As Jacobi (134) has shown in a beautiful series of roentgenographic studies, the most common result of chronic pyelitis extending through a series of pregnancies with exacerbations during the pregnant periods is the "fixed" fibrosed ureter and kidney pelvis, the fixation being due to fibrosis in the dilated state, so that the end-

result is hydronephrosis and hydro-ureter. This pathological change, of course, precludes anything simulating a return to normal peristaltic activity on the part of the kidney pelvis and ureter.

In view of what has been learned, largely as a result of the work of Creevy (59) and Wuellenweber (327), concerning the importance of the ureter as a pumping mechanism which normally keeps the intrapelvic pressure at a level below that in the bladder and thus avoids back pressure upon the renal cortex, one can visualize what damage permanent decompensation of the ureter may attain. In fact, there are those—Walker (315), Peters (225), and Hayes (110)—who are of the opinion that these changes bear a relationship to the transitory hypertensive toxemias of pregnancy and even hypertension of later life. The theories and the clinical data these authors present are suggestive and should stimulate further inquiry; however, they cannot be considered conclusive.

Robecchi (246) reports a follow-up study in which he analyzed the results of pyelitis from five to thirty months after the acute attack. Only 23 per cent of the patients were found to be normal in all respects. The other 77 per cent showed albuminuria, pyuria, bacteriuria, and all had some degree of hydro-ureter. None of the patients showed reduced renal function.

Haselhorst (109) studied 62 women after they had pyelo-ureteritis and found minor difficulties in 39, while 19 had exacerbations of the inflammation, and 3 had developed hypertension. He concludes, "pyelitis gravidarum is not the harmless disease which always heals itself spontaneously, postpartum, as is so often claimed, but it is, in a great many cases, active silently over a long period of years and forms a latent danger which can assume different forms."

Dodds (75) reports death in 1.6 per cent of his cases. In the postnatal follow-up of 124 patients, 27 had chronic pyelitis, 20 had bacteriuria alone, and 42 seemed quite well. Grieve (102) writes of his studies of 37 women some months after delivery. One had died of urinary complications, while 23 were found to be quite well. Eight, or 21 per cent, had failed to throw off the disease and suffered "impaired health" as a result of the latent chronic infection which they still were harboring.

These results are presumably what may be expected from the older methods of treatment. They indicate ample room for improvement in the net result. This improvement now seems entirely possible, as will be indicated in the section on treatment.

EFFECTS OF PYELO-URETERITIS OF PREGNANCY ON THE INFANT

As long ago as 1904, Cathala (31) made the following statement: "The prognosis for the child is grave (in pyelitis of pregnancy), as delivery may be premature, and infection may be transmitted to it." We have been slow in learning that prolonged treatment of the mother during the acute or subacute phase, in the hope of gaining a viable infant, may end in disappointment. Haselhorst (109) gives the fetal mortality as 10 per cent, while Traut (298) found it to be 12 per cent during a period in which the total fetal mortality from all causes, including pyelitis of pregnancy, was 4.2 per cent. These reports are in line with those of other observers.

The cause of fetal death is often due to prematurity. In Freudenberg's (88) report the incidence of premature delivery was 16.1 per cent, and Baird reports premature parturition in 40 per cent of the primigravidas, and in 15 per cent of the multiparas.

Intra-uterine death also occurs, though less frequently than premature birth, the only figure obtainable being 8 per cent (Traut, 298), while neonatal death occurs in 5 per cent of the cases. As pointed out by De Beaufond (70), intra-uterine and neonatal death referable to the infection of the urinary tract is due to bacteriemia, the infant becoming infected by passage of the colon bacilli through the placenta. De Beaufond reports that one infant survived, even though it had positive blood cultures for four weeks post partum. Athenstaedt (4) gives a good review of the literature up to 1933 on this subject.

TREATMENT

The very real advances which have been made with regard to the treatment of pyelo-ureteritis are those which have come as a result of a more complete understanding of the history of infections in the upper urinary tract in the adult woman. This understanding focuses attention upon prophylactic care as the greatest hope in amelioration of the effects of this disease, toward which the normal physiological changes of gestation predispose, on the one hand, and, on the other, which dictates the necessity for urological treatment in its chronic stages following the initial attack, once it appears.

It is quite essential in the approach to the subject of treatment to understand that the acute febrile exacerbations are merely the very obvious high spots of the disease process, and that usually following such episodes there are much longer—because they are chronic and asymptomatic—

stages of infection which must be managed effectually. Treatment confined to the acute, febrile stage begs the question and bespeaks a lack of insight. For this more complete point of view, we are indebted to those students of the disease who have observed it critically over a considerable period of years, among whom must be named particularly Stoeckel, Weibel, De Beaufond, Baird, Kretschmer, and Crabtree.

The following remarks on treatment are made with the feeling that much of what is said may soon need revision because of the advent of sulfanilamide therapy. However, the use of that drug in its various forms is in such a chaotic state as to make assessment of its true value impossible at the present time.

Treatment of the acute phase in pregnancy. All writers agree that for a period of four or five days, patients should be treated conservatively according to the simple formula of rest in bed with frequent changes of position, forced fluids, saline catharsis, soft diet, and therapy to render the urine either strongly alkaline or acid. As over 60 per cent of the patients respond to this simple regimen, it is worth while to continue its use. If loss of fluids by emesis or inability to take fluids by mouth is a feature of the disease, parenteral replacement is of the greatest importance. At the same time, a careful history should be taken to discover the possibility of previous attacks, and bacteriological cultures of the urine are desirable because they will reveal the type of organism, while blood chemical evaluation of the non-protein-nitrogen level and some form of differential kidney-function test (the intravenous pyelogram being the simplest and most useful), should be carried out. These latter procedures will show whether a mixed infection is present, whether the renal cortices are involved dangerously, and whether previous kidney damage in one or both kidneys has been sustained. All these factors alter the prognosis, and, hence, the degree of conservative treatment that is justified.

With this data in hand the physician is prepared to meet the complications which arise. If the acute attack be established by the history to be a recurrent one, or if the infection be a mixed one, the assumption that the patient may not respond promptly to simple therapy and also that serious complications may occur is justified. If diminished kidney function is present in the kidney not involved in the acute attack, caution is indicated. In bilateral pyelo-ureteritis and in the presence of a rising nitrogen level in the blood, associated with oliguria and leucine and tyrosine in the urine (Philipp 229), extreme caution is necessary and usually prompt evacuation of the uterus is indicated.

If after the initial period of the conservative therapy outlined above, lasting from four to seven days, the temperature remains elevated, more active treatment is indicated. It is usually advisable that the indwelling ureteral catheter of large size be used in the attempt to establish more adequate drainage. When the response to this form of treatment is not satisfactory, a day or two of rest and then re-insertion may be advised, it being presupposed that none of the more serious complications have developed.

Mandelic-acid therapy as developed by Rosenheim (251) and Helmholz (116) is usually inefficacious during pregnancy, and probably should never be used in the acute phase. However, it has been most useful post partum in the clearing up of chronic infections. Dosage should approximate 12 gm. of the drug daily, in divided doses, with fluids limited to 1,500 c.cm. and sufficient ammonium chloride by mouth to render the urine very strongly acid to methyl red as the indicator. There are many recent reports (Helmholz, 116, Long, 182, Cook, 45) stating that sulfanilamide by mouth in dosage ranging from 1.5 to 6 gm. per day is valuable. This substance is said to have a decided advantage over any other urinary antiseptic in that it is effective in an alkaline urine, whereas mandelic acid, beta-oxybutyric acid, and other substances are bactericidal only in an acid medium. In addition, sulfanilamide has been shown to penetrate all tissues of the body about equally, with the exception of the bony skeleton and brain, so that it is not merely a substance working on the surface of a hollow viscus as are most other so-called urinary antiseptics.

Fortunately, most patients respond to the above treatment or some modification of it. However, there will be a few who fail to improve under any conservative therapeutic regime, and in these cases the physician must face the necessity of terminating the pregnancy. Only a few writers fail to agree with this point of view. Most of them hold not only that the termination of pregnancy is a life-saving procedure that must occasionally be used, but also that, if the fetus be several weeks from term, irreparable damage may be sustained by the mother if evacuation of the uterus is not carried out. The knowledge that the infant may be lost, regardless of the course followed, is an added indication for considering the mother and her future welfare of primary importance. In the statistics of the Kiel Frauenklinik (88), the incidence of therapeutic interruption of pregnancy was 7.7 per cent.

Treatment of the acute phase occurring in the puerperal woman is a much simpler problem, as adequate drainage can usually be secured, and one is at liberty to use non-irritating antiseptics, such as sulfanilamide, at once.

Effective treatment of the chronic stages of the disease has, in the past, required some facility with urological technique. However, if the recent experience of Helmholz (117), Long (182), and others with sulfanilamide is borne out by prolonged trial, it may be possible greatly to simplify the treatment by elimination of the necessity for ureteral catheterization. In general there are three objectives to be attained in the treatment of chronic infection of the urinary tract, namely, eradication of the causes of residual urine in the bladder, ureter, or kidney pelvis; cure of the infection; and avoidance of pregnancy until the two former have been accomplished.

Crabtree (57), has shown that with the best available care in the presulfanilamide era, patients having had pyelo-ureteritis respond and are usually cured within four months post partum. If they are not cured under these circumstances, the cause is usually debility, abnormal persistence of ureteral changes incident to pregnancy, or bladder damage with residual urine.

As stated above, ammonium mandelate in dosage of 12 gm. of the drug per day during periods of seven days has been found to be of great assistance in clearing up the chronic infections.

Long (182) has elaborated a technique for the use of sulfanilamide which is calculated to attain certainty in the use of this drug. It has been shown that individuals vary markedly in their ability to excrete the unconjugated fractions of the drug (Marshall, 195); therefore, Long has found it necessary to determine the amount they can eliminate through the kidneys and then provide dosage sufficient to afford the degree of saturation which he has previously demonstrated as necessary to kill the offending organism *in vitro*. It is to be hoped that, as a result of these and similar well controlled investigations, general rules for the use of sulfanilamide may be developed, which will make its use more simple as well as certain and safe. Thus far, we have not arrived at a well authenticated method for the use of sulfanilamide. It seems wise to consider this form of therapy as distinctly in the experimental stage and, therefore, not to be recommended at this time without definite reservations.

The criteria for cure of chronic pyelo-ureteritis should consist of a series of three negative cultures of bladder urine, separated by intervals of at least one month.

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GYNECOLOGY

UTERUS

Taylor, H. C., Jr., and Millen, R.: The Causes of Vaginal Bleeding and the Histology of the Endometrium After the Menopause. *Am. J. Obst. & Gynec.*, 1938, 36: 22.

Among 406 gynecological cases admitted to the Roosevelt Hospital, New York, for vaginal bleeding after the menopause, some type of malignant tumor was present in approximately 63 per cent.

Benign tumors of the uterus and ovary were the lesions chiefly responsible for the symptom in 17 per cent of the cases. Of special interest was the association of hyperplasia of the endometrium with typical cystic pseudomucinous tumors of the ovary in two instances.

Inflammatory lesions, usually in the cervix or vagina, were the apparent cause of bleeding in 11 per cent.

In the remainder, or about 8 per cent, no gross lesion to explain the bleeding was present in the pelvis. Several of this group showed evidence of a late ovarian effect on the endometrium or of an endometrial hyperplasia due to this or other causes. These instances of hyperplastic changes in the postmenopausal endometrium are important as possible precancerous lesions. EDWARD L. CORNELL, M.D.

Phaneuf, L. E.: Irradiation in the Treatment of Carcinoma of the Uterus, with Special Reference to Corpus Carcinoma. *Am. J. Roentgenol.*, 1938, 39: 855.

The history of gynecology has been written around the treatment of uterine carcinoma. During the last two decades irradiation with radium and roentgen rays has supplanted surgery in the treatment of cervical cancer. No such radical change has taken place in the management of cancer of the uterine body. Surgery, in the form of a panhysterectomy with the ablation of the adnexa, has given five-year arrests in from 60 to 70 per cent of the cases in some series. Irradiation has been reserved, for the most part, for patients advanced in years, having definite contra-indications to operation because of constitutional lesions and because of the advanced stage of the disease. Even in this group arrests have been observed, and the palliation obtained in others has been beneficial. The use of pre-operative radium irradiation and surgery, and postoperative deep roentgen therapy may improve the results of the future. A small series of 20 cases of corpus carcinoma treated by irradiation is presented in the form of a preliminary report.

In this group of cases the oldest patient was seventy-eight years, and the youngest forty years. A hysterectomy was performed on the youngest woman four months after intra-uterine application of radium. All others were treated by irradiation alone. Two patients are alive and free from recurrence for more than seven years, 1 patient is alive and free from recurrence for more than six years, 1 patient who was free from recurrence more than six years after the initial treatment, died of diabetes, and 1 patient is alive and free from recurrence for more than five years. Thus, 5 patients, or 25 per cent, survived more than five years. Five patients, or 25 per cent, are known to have died from cancer; 3 patients, or 15 per cent, cannot be traced, and the 7 others, or 35 per cent, have been under observation less than five years.

J. THORNWELL WITHERSPOON, M.D.

Corscaden, J. A., Kasabach, H. H., and Lenz, M.: Intestinal Injuries after Radium and Roentgen Treatment of Carcinoma of the Cervix. *Am. J. Roentgenol.*, 1938, 39: 871.

In the records of 350 cases of carcinoma of the cervix and of 92 cases of fundal carcinoma treated with radium and x-rays, symptoms related to the lower alimentary canal were noted in 139 patients. The observed conditions ranged from the simplest proctitis to more severe inflammation in 16 cases and to ulceration in 12 cases; there was cicatricial stenosis in 1 case and perforation in 5 cases. Fifteen cases illustrating the more serious of these complications are reported in detail. While the technique of treatment and the dosage were not uniform, the following standard was approximated in all:

Radium factors. Radium tubes were placed in tandem in the cervico-uterine canal in sufficient numbers to occupy the length of the canal. Filtration was secured with 1 mm. of platinum plus 1 mm. of rubber. Three vaginal applicators were placed, one against the cervix, and one in each lateral fornix. The filtration was the same as already mentioned plus 5 mm. of cork, rubber, or gauze. The bladder and rectum were firmly forced away by gauze packing. The total dose was usually given in one or two applications. The applicators, containing a total of 175 mgm., were left in place about forty hours, which produced a total dose of approximately 7,000 mgm. hr.

Roentgen-therapy factors. Two hundred kilovolts, 50 cm. distance, 1.5 mm. of copper or 2 mm. of copper plus 1 mm. of aluminum filtration. Between 300 and 400 roentgens were given each day, through several fields. The duration of the course was from twenty-one to thirty days.

The authors believe that the alimentary symptoms observed, ranging from nausea and diarrhea to gross necrosis and perforation, were due to a true radiation enterocolitis rather than to a more general intoxication. In 16 cases abdominal cramps and diarrhea with mucus and blood streaks in the stools suggested a more intense irritation. The mucosæ of the rectum and sigmoid were swollen, red, and dotted

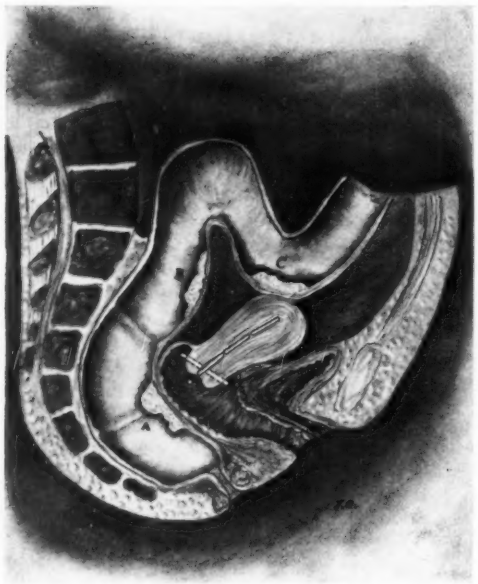

Fig. 1. Diagram showing the sites of injury in the lower bowel: *A*, in rectum adjacent to vagina; *B*, rectosigmoid at some distance from cervix; *C*, a loop of sigmoid adherent to fundus.

with numerous punctate hemorrhagic spots. Spasm of the rectosigmoid was present in 6 of the patients in this group. These manifestations were a continuation of those experienced during treatment and lasted up to four months. All of the patients healed spontaneously.

Ulceration occurred in the rectum (Fig. 1A) in 4 cases; in the rectosigmoidal region (Fig. 1B) in 4 cases; in the loop of the sigmoid (Fig. 1C) in 2 cases; and in the small intestine in 2 cases. The symptoms were abdominal cramps, diarrhea, and frequent and bloody stools. Those occurring in the large bowel usually presented themselves several months after the termination of treatment. In the rectal cases recovery was spontaneous after from two to twelve months. In the cases of ulcer of the rectosigmoidal region, 2 patients recovered spontaneously after some months, and the other 2 died following colostomy to relieve obstruction. Both patients with ulcers in the loop of the sigmoid developed obstruction. One survived a colostomy and the other did not. In the 2 cases in which severe injury to the small intestine occurred the symptoms were continuous with those arising during treatment. Both patients died within two months. A diffuse fibrinopurulent peritonitis without perforation was present.

Rectovaginal fistula occurred in 5 cases. All of the fistulas were accompanied by the continuance of the carcinoma.

Some of the patients were studied roentgenologically after having had repeated barium enemas. In the more severe cases, varying degrees of stricture, spasm, and exaggeration of the mucosal folds were observed.

The treatment of the ulcers was palliative until signs of obstruction appeared. Paregoric and a bland diet were of value. Operative treatment of the obstruction was satisfactory when simple colostomy could be performed. When an attempt was made to remove the affected area, the result was unsatisfactory.

Several forms of cicatricial deformity of the rectum were observed:

1. A leathery ridge 6 or 8 cm. from the anus, extending laterally to the pelvic walls, due to contraction of the parametrial tissue. There were no symptoms. This deformity is of interest because it is difficult to distinguish it from carcinomatous extension.

2. An annular stricture without previous ulcer. This was observed once.

3. Atrophy of the mucosa of the anterior rectal wall over an area of 5 or 6 cm. This was observed frequently. The only symptom was occasional streaks of blood in the stool.

4. The healing of the ulcers described, which left a puckered scar.

The authors wish to emphasize the importance of the time factor in dosage. Radiation injuries have practically been eliminated in their cases without reduction of either the total milligram-hours or roentgens administered. This was accomplished by reducing the number of milligrams used in the uterovaginal applications from 175 to 70 and increasing the duration of the application from forty to one hundred hours; and by reducing the daily roentgen dose from 300 to 400 roentgens to 100 to 200 roentgens, and the size of the field from 20 by 20 cm. or 15 by 20 cm. to 10 by 15 cm. or less, and increasing the duration of the course of treatment from twenty-one to thirty, forty or more days. The variation in dosage is determined by the occurrence of alimentary symptoms and the susceptibility of the skin. Severe diarrhea, nausea, and abdominal distress are considered as warnings of possible bowel injury. The adoption of this technique by the authors has decreased the incidence of bowel injuries from 8.7 per cent to practically nil.

DANIEL G. MORTON, M.D.

Frazell, E. L.: The Correlation of Calculated Tumor Doses and Five-Year Survivals in Radiation Therapy of Cancer of the Cervix. *Am. J. Roentgenol.*, 1938, 39: 861.

The prognosis for a five-year cure of carcinoma of the cervix depends to a large extent on the clinical stage of the disease when treatment is started. There seem, however, to be other factors that influence the prognosis. The importance of the histological type of the tumor and of the age of the patient are debatable. The author believes that the degree of ade-

quate irradiation of the tumor is of utmost importance as to the final prognosis.

The author studied 136 patients with carcinoma of the cervix treated by irradiation during the year 1930. Most of the patients in this series were treated by preliminary roentgen radiation through four pelvic fields; one or two weeks later radium was applied locally, and about twelve weeks still later a second roentgen cycle was begun.

The minimum dose of irradiation given to each tumor was then calculated in terms of threshold erythema doses. These calculated doses were then correlated with the five-year end-results. It was found that patients receiving less than 3 threshold erythema doses had a five-year survival rate of 16 per cent, those receiving from 3 to 6 doses a rate of 24 per cent, those receiving from 6 to 9 doses a rate of 22 per cent, those receiving from 9 to 12 doses a rate of 47 per cent, and those receiving more than 12 doses a rate of 67 per cent.

On the basis of this data the author concludes that it is essential to use high threshold erythema doses of irradiation in therapy of carcinoma of the cervix. Methods should be found to increase the irradiation dose to the parametria without causing irreparable damage to vital structures. Any method of radiation therapy delivering less than 6 erythema doses to the parametrium will fail to control the disease in the majority of cases.

RONALD R. GREENE, M.D.

EXTERNAL GENITALIA

Te Linde, R. W.: The Treatment of Gonococcic Vaginitis with the Estrogenic Hormone: Further Studies. *J. Am. M. Ass.*, 1938, 110: 1633.

Te Linde reports success with the use of amniotin in the treatment of 175 patients with gonococcic vaginitis. All, except 16 to whom the product was given hypodermically in oil, were cured by the use of amniotin vaginal suppositories. No patient who has failed to benefit from this treatment has yet been encountered. The first 100 patients who had undergone treatment were seen after from three months to two and one-half years and 98 of them were found to be well. No clinical evidence of any harm due to the treatment was found, and laboratory investigations have confirmed this observation. The increased acidity which takes place in the vagina as a result of the action of the estrogen is a factor in overcoming the infection. Since results were not nearly so good when another acidifying suppository was used, it is believed that amniotin introduces an additional curative factor. Te Linde is of the opinion that this factor is the covering of the vagina with thick epithelium, which prevents reinfection of the subepithelial tissues and thus permits the inflammatory process in them to subside. Clinical observations and biopsies have indicated that the essential lesion of gonococcic infection of the lower part of the genital tract in female children is vaginitis.

CHARLES BARON, M.D.

Wharton, L. R.: A Simple Method of Constructing a Vagina. *Ann. Surg.*, 1938, 107: 842.

A new operation for the construction of a vagina is presented. It is based upon the remarkable ability of the vaginal epithelium to proliferate and cover raw surfaces. This is essentially the manner in which the vagina develops in the fetus.

After an incision is made into the external mucous membrane, or across the dome of the rudimentary vagina, a space is dissected between the bladder and the rectum by blunt dissection. It is only necessary to follow the plane of cleavage provided by the fibro-areolar tissue between the layers of subvesical and perirectal fascia. Into this newly created space is introduced the vaginal mold, covered by a condom, which completes the operation. The mold is essential as a means of keeping the vaginal space open so that the vaginal epithelium may cover it. The ideal mold should be very light so that it will not cause any pressure on the surrounding organs, and it should be firm so that its shape may be preserved against the continual pressure of the pelvic muscles and the surrounding structures. Molds of balsam wood or of melted paraffin have proved most satisfactory.

The mold is allowed to remain in the vagina for a period of three weeks. During this time it requires no attention other than that of making certain that it does not come out. The patient is kept in bed as long as the condom is in place. Coitus is absolutely prohibited for a period of at least two or three months, or until the vaginal epithelium has become thick and tough.

This operation seems feasible only when some vaginal epithelium is present.

CHARLES BARON, M.D.

MISCELLANEOUS

Pieri, R. J.: The Female Perineum: Episiotomy and a Technique for Its Repair. *J. Am. M. Ass.*, 1938, 110: 1738.

As a result of excessive strain during labor, overstretching or laceration of the muscles of the perineum frequently occurs. This is invariably accompanied by single or multiple tears in one or more of the various layers of pelvic fascia, which in many places is in such intimate relation to the perineum as to be considered a part of it. These injuries, by weakening the support of the pelvic organs, constitute one of the chief factors in the production of such sequelæ as cystocele and rectocele.

In performing an episiotomy, the advantages to the baby lie chiefly in the shortened period of pounding of the fetal head on the perineum and the consequent reduction in the incidence of cerebral injury. As for the mother, the second stage of labor is shortened, while the restoration of the pelvic floor after episiotomy, properly performed, is usually better than that which is observed even after many normal deliveries in which no visible lacerations

occur, the integrity of the soft parts often remaining as unimpaired as they were in their nulliparous state.

In the absence of any indication for earlier intervention, delivery is not attempted until the presenting part is on the levators and there is evidence of pressure on the vulvar outlet. After the usual preparation for delivery, the bladder is catheterized and the perineum gently "ironed out" with the liberal use of neutral liquid soap. Care should be exercised to avoid overstretching of the parts and too rapid dilatation. The former causes future loss of muscle tone and damage to the fascia, while the latter favors laceration.

The site of incision depends on the operator, the right or left mediolateral episiotomy being favored by most accoucheurs chiefly because it avoids the rectum. The point of direction extends from the midpoint of the posterior aspect of the vaginal orifice and proceeds along a line midway between the sphincter and the ischial tuberosity.

The technique of repair causes a minimum amount of postoperative discomfort. All sutures are of a fine texture and coincide with Harvey's opinion "that it is never necessary to use any suture stronger than the tissue through which it passes." Single sutures are preferred to double sutures, since the difference in their holding strength is practically negligible.

The first layer of sutures (chromic No. 1) is interrupted. The sutures are passed widely to reduce tension on the line of healing, and tied just securely enough to secure coaptation. Care is observed, of course, to avoid perforation of the rectum. The first stitch is submucous and is passed in circular fashion around the upper angle of the incision. This brings together any fibers of muscle or fascia which might have separated under the mucosa. Neglect in this detail favors subsequent "pouching" of the posterior vaginal wall, or even a later rectocele, if such an occult separation exists.

The second layer of sutures includes the fascia of Colles. No. 0 chromic gut is selected because of its ample strength (8 lb.) in fascia. It is at this time that the "crown" stitch is inserted, which brings together the severed portions of the hymen, the needle being inserted obliquely upward in the base of the labia minora to secure in its grasp the retracted fibers of the severed constrictor cunni (bulbocavernosus) muscle. To overcome this retraction and to prevent gaping of the vagina, two such sutures may be required. To avoid "dead space" any muscle underlying the fascia is included in the bite of the needle as it is passed from one side to the other.

When completed, the second layer usually brings into apposition the edges of both the mucosa and the skin, respectively. Frequently, however, to insure this, a third or subcuticular layer of double 0 or triple 0 catgut is placed, a fine skin needle being used. No sutures are passed through either the vaginal mucosa or the skin, and those portals of entry which invite pathogenic organisms from without to follow the suture into the tissues below are thus eliminated.

As a final step the line of incision is effectively sealed by gentle coaptation of its everted edges by means of Allis clamps. These are applied and permitted to remain clamped for only a few moments while the vaginal packing is removed, any blood clots are expressed, and preparations are completed for the transfer of the patient to her bed. Removal of the clamps leaves a fine linear scar which, for a brief interval, remains elevated as a result of the eversion, and then becomes almost imperceptible as the elevation recedes.

No case of infection or "breaking down" of the perineum has been observed in the present series of more than 400 cases. CHARLES BARON, M.D.

Fabre, M., Papillon, F. A., and Pecker, A.: The Treatment of Gonorrhea of the Female Reproductive System (Les traitements de la blennorragie génitale de la femme). *Rev. franç. de gynéc. et d'obst.*, 1938, 33: 321.

The authors point out that it is frequently difficult to find the gonococcus in the female generative tract. The treatment of gonorrhea in the female, therefore, is often intricate and requires considerable patience and perseverance on the part of the physician. The clinical picture and the bacteriological findings should be constantly correlated in outlining the course of therapy.

Fabre, Papillon, and Pecker divide the most commonly used therapeutic methods for gonorrhea in the female into two general groups: (1) local therapeutics, either medical or surgical, and (2) systemic therapeutics.

In considering local treatment, the authors discuss the various procedures employed in the therapy of gonorrheal vulvitis, vaginitis, bartholinitis, and urethritis. These consist essentially of irrigations with potassium-permanganate solutions and the application of silver-salt preparations. Chronic gonorrheal cervicitis may be treated medically by the application of silver salts or by other forms of chemical cauterization, or by surgical methods, such as electrocoagulation of the cervix, trachelorrhaphy, and cervical amputation.

Gonorrhea usually also produces a chronic endometritis which, however, shows a tendency toward spontaneous healing. It may be treated by curettage followed by the topical application of zinc sulfate or silver salts. It should be remembered, however, that in cases of acute gonorrheal endometritis, intrauterine manipulations should be strictly avoided.

Gonorrheal salpingo-oophoritis and pelvic peritonitis should be treated systemically by means of vaccinotherapy, chemotherapy, or proteinotherapy. All surgical interventions in these conditions are positively contra-indicated unless there is an accumulation of pus in the cul-de-sac, in which case a colpotomy should be considered. In chronic cases of pelvic peritonitis with involvement of the adnexa,

the authors recommend vaccinotherapy, diathermy, and short-wave therapy. Surgical methods are gradually being eliminated.

The authors then discuss physiotherapeutic measures which are used in gonorrheal vulvitis, vaginitis, urethritis, endometritis, salpingo-oophoritis, and pelvic peritonitis.

In recent years vaccinotherapy has come to the fore but the authors believe that this form of therapy, if employed alone, does not offer permanent relief from gonorrhea or its complications.

Other therapeutic measures which have been employed in the treatment of gonorrhea in the female include serum therapy, hormonotherapy, diathermy, and short-wave therapy.

Concerning chemotherapy, for several years the intravenous administration of acridine derivatives has given some highly promising results but, unfortunately, the method has not found general acceptance and has been practically abandoned at present.

During the past year sulfanilamide therapy has come into general use. With elevated dosage, it has yielded noteworthy results in the treatment of gonorrhea, but according to a review of the literature made by the authors, it has also caused many accidents. When employed with low dosage and in combination with other therapeutics, its efficacy is still questionable. In spite of its disadvantages, this form of therapy is highly promising. Among the most common untoward reactions observed in connection with sulfanilamide are disturbances such as skin eruptions, headache, asthenia and dizziness, digestive disturbances, subicteric states, anemia, cyanosis, and menorrhagia.

Among a series of 103 patients receiving sulfanilamide (1162 F) there were observed 46 adverse reactions in 37 patients. In another series of 50 patients receiving rodilone [1399F; di (para-acetylaminophenol) sulfone] there were observed 31 adverse reactions in 26 patients.

Sulfanilamide derivatives are indicated in gonorrheal vulvovaginitis, bartholinitis, urethritis, cystitis, cervicitis, endometritis, and gonorrheal involvement of the adnexa. RICHARD E. SOMMA, M.D.

Turunen, A.: External Endometriosis and Sterility (Endometriosis externa and Sterilitaet). *Acta obst. et gynec. Scand.*, 1938, 18: 237.

The author concludes that external endometriosis is an extremely important cause of sterility. He bases this conclusion on a study of 159 operatively proved and corrected cases in the gynecological clinic at Helsingfors during the period from 1930 to 1936.

There were 113 married women in this group and, reckoning the normal period between births of the Finnish married woman as three and one-tenth years (Kahanpää), 48 (42.5 per cent) of these women had been without a pregnancy for approximately three years and were probably primarily sterile. Fifty-six (49.5 per cent) had had one or more children, but at the time of operation had not been pregnant for approximately three years and were secondarily sterile. Of the 9 women reckoned as fertile, 5 were not known to be actually fertile, as they had had no pregnancies since marriage; they had merely, at the time of operation, not yet been married for three years.

The condition in 66 of these women (34 primarily and 32 secondarily sterile) could be corrected by a conservative operation, by loosening of the adhesions, excision of endometriosic foci, or reperitonealization, and 21 (12 of the former and 9 of the latter) later became pregnant, most of them within the first year. Therefore, a considerable number of women who were sterile in the presence of external endometriosis were relieved by conservative operation, and the author believes that the attempt should be made to diagnose this condition sufficiently early that conservative measures may be used in its treatment. Recurrence following this operation is extremely rare. JOHN W. BRENNAN, M.D.

OBSTETRICS

PREGNANCY AND ITS COMPLICATIONS

Mahfouz, N. P.: Ectopic Pregnancy. *J. Obst. & Gynaec. Brit. Emp.*, 1938, 45: 209.

In this article the subject of ectopic pregnancy is considered in full and the comments are supported by observations upon 120 cases. The following etiological factors are discussed: distortion of the lumen of the tube by peritoneal adhesions, the formation of blind pockets by the adhesion of adjacent mucosal plicæ incident to inflammation and its subsequent healing, delay in the downward passage of the ovum due to tubal stenosis or to inefficiency of peristalsis, and interference with the passage of the ovum caused by mucosal polypi or by the pressure of tumors in the wall of the tube or in adjacent organs. Sixty-five of the author's patients were over thirty years of age, and more than half gave a history of previous salpingitis and sterility.

Of the 120 cases, 4 were tubo-abdominal (secondary abdominal), 1 was ovarian, 1 was primary abdominal, and 5 occurred in a rudimentary uterine horn. The remainder were definitely tubal, the vast majority occurring in the ampullary and isthmian portions. Rupture into the peritoneal cavity occurred in 58 per cent (in some cases after death of the fetus); intratubal rupture occurred in 27 per cent; and rupture into the broad ligament occurred in 5 per cent. In 11 patients, pregnancy advanced to the later months; of these only 1 came for treatment while the child was alive and viable. In 3 of the 11 cases, pregnancy occurred in the ampullary portion of the tube and proceeded to term without rupture.

The rare varieties of ectopic gestation, the interstitial, the ovarian, and the abdominal, are discussed in some detail. Attention is called to the relatively high incidence of fetal abnormalities in cases of ectopic pregnancy. Probably this is due to nutritional deficiency induced by faulty placentation. When the fetus is not removed, it becomes mummified or calcified. Lithopedions were found in 3 per cent of the author's cases.

The four cardinal symptoms of ectopic pregnancy, viz., amenorrhea, repeated attacks of pelvic pain, irregular uterine hemorrhage, and the passage of a decidual cast, were seldom present together in the author's series. Pain was present in 65 per cent, irregular hemorrhage in 70 per cent, and amenorrhea in 35 per cent, and passage of a decidual cast occurred in 25 per cent. The differential diagnosis is discussed.

In the rare cases in which the diagnosis of unruptured tubal pregnancy is made, the gravid tube should be removed without delay. Occasionally a more conservative operation may be done: the alternative is salpingotomy with enucleation. Although the possibility of a repetition of pregnancy in the same tube is recognized, the author believes that this operation is indicated for certain young women who are very desirous of bearing a child. For interstitial pregnancies, hysterectomy is usually the safest procedure. When hemorrhage is diffuse and the patient's condition is poor, immediate operation is indicated. Infusions or transfusions are indicated only after the operation has begun. In the event of small encysted hematoceles which are not enlarging, the patient may be treated expectantly. Operation should be performed, however, if the hematocele is enlarging or is already very large, or if the Aschheim-Zondek test remains positive.

For advanced ectopic pregnancy, immediate operation is advised whether the fetus be alive or dead. The danger of removing the placenta depends upon its location and not upon whether the fetus is living or dead. When an advanced tubal pregnancy exists, there is no difficulty. If a secondary abdominal pregnancy exists, the danger is great. The proper method of managing the placenta depends upon circumstances. In 1 case the placenta was peeled off without important hemorrhage. In a second case, the placenta was left in place, and a subsequent laparotomy revealed it to have been completely absorbed. A third patient, in whom the placenta was marsupialized, died.

The mortality of the 120 cases was slightly less than 2 per cent. The article is accompanied by excellent illustrations. DANIEL G. MORTON, M.D.

Brandstrup, E., and Okkels, E.: Pregnancy Complicated with Diabetes. *Acta. obst. et gynec. Scand.*, 1938, 18: 136.

Twenty-two instances of pregnancy in 19 diabetic patients were observed in the lying-in department of the Rigshospital in Copenhagen. Of 23 children, only 10 were discharged from the hospital alive. Six were stillborn with third-degree maceration, 2 were excessively large and died during delivery, and 5 died in the first days after birth. Two of the last group were born prematurely. In no case was hypoglycemia proved to be a cause of death. The high infant mortality may probably be attributed to maternal hyperglycemia and acidosis. In 3 instances changes observed at necropsy in the pancreas, hypophysis, and thyroid are described.

No clinical evidence was found of any permanent change in the severity of the maternal diabetes as the result of pregnancy. Acidosis was frequent and variations in insulin dosage were necessary, but these were temporary and ascribed to exogenous factors. Precomatose conditions or coma appeared in 6 of the 22 women. Phenomena of insulinism were observed in 13 patients, not infrequently in connection with hyperemesis and a lowered state of nutrition. The insulin requirement decreased in 6, increased in 4, and remained unchanged in 8 patients; no insulin was given in 4 instances.

Pregnancy obviously adds to the danger and difficulty of the management of diabetes. The obstetrical risk is somewhat increased through a tendency toward hydramnios, excessive size of the child, and especially infection when eczema of the vulva is present. The chief aim of future treatment must be to make obstetrical operations unnecessary by means of medicodietetic management. The pregnant diabetic patient must be watched very closely and efforts made to avoid hyperglycemia and acidosis. With the new insulin it is hoped that great variations in the blood-sugar concentration can be avoided and that the prognosis for the diabetic mother, and especially for her child, can be improved.

WALTER H. NADLER, M.D.

LABOR AND ITS COMPLICATIONS

Insulander, M.: The Relief of Pains in Childbirth. *Acta obst. et gynec. Scand.*, 1938, 18: 179.

The author reviews her impressions of 23 Lying-in Hospitals which she visited in the United States. A great many medicinal substances were employed to alleviate the pains in childbirth, even at an early stage of the delivery. This applied chiefly to the private hospitals, the municipal hospitals not having at their disposal a large enough staff for continued supervision of the patient.

Barbituric-acid preparations, the combination of morphine and scopolamine, and paraldehyde were the preparations most frequently used. All of them give good amnesia and do not lessen the effect of the labor pains. Many patients, however, become very agitated, and the number of artificial deliveries is increased. Furthermore, the children frequently become apathetic.

The increased number of artificial deliveries renders unsuitable the introduction of the American preparations into Sweden. Their employment is possibly adapted to the very active American obstetrics. Even in some quarters of the United States there is to be found a marked reaction against the wide-spread use of analgesics in childbirth.

In England laughing gas was used to a large extent. It is administered with an apparatus controlled by the patient herself. It was the method that seemed to give the best promise for the future.

In Germany ether or chloroform was used almost exclusively. Other preparations were considered too dangerous.

CHARLES BARON, M.D.

Leidenius, L.: Causes of Death at Childbirth. Statistical Study from the Gynecological-Obstetrical Clinic at Helsingfors (Ueber die Ursachen der Partussterblichkeit. Statistik der Frauenklinik in Helsingfors). *Acta obst. et gynec. Scand.*, 1938, 18: 24.

This article is based on 47,793 deliveries at the University Clinic at Helsingfors. The author divides these deliveries into two ten-year periods, from 1914 to 1923, and from 1924 to 1933, this division tending to suggest that no considerable reduction in the causes of morbidity had been attained in spite of all efforts. Of the patients, 0.45 per cent and 0.38 per cent, respectively, died, about half of the deaths in each period being due to infection. However, the great majority of the infections were present before the patients entered the clinic.

The author believes that further reduction of the mortality can best be attained by prophylaxis, especially in the infectious and toxic cases (23.7 and 27.1 per cent, respectively), and by proper care during pregnancy of the patients with weak hearts (12 per cent of all the patients who died during the second ten-year period). Financial assistance and the establishment of stations for childbirth, within easy reach of every pregnant woman, are also suggested.

JOHN W. BRENNAN, M.D.

PUERPERIUM AND ITS COMPLICATIONS

Fortin, F. F.: A Comparative Study of Posterior Pituitary Extract Administered at the Onset of and After the Completion of the Third Stage of Labor. *Am. J. Obst. & Gynec.*, 1938, 35: 761.

The optimum time for the administration of pituitary extract in controlling post-partum bleeding is an unsettled question. A comparative study of the prophylactic administration of pituitary extract in the third stage of labor, and after completion of the third stage, is presented. The author's study involved 1,100 cases in each series and the results obtained are as follows:

1. The general average blood loss and the group percentage distribution are too nearly alike to concede an advantage to either method.

2. The investigation of induced and stimulated labors yielded inconsistent results.

3. There is a 5.5 per cent reduction of the blood loss in normal cases and a 6 per cent reduction of the average loss of blood in operative cases when pituitary extract is administered prophylactically. The maximum saving is less than an ounce.

4. Prophylactic administration reduced the incidence of post-partum hemorrhage by 2.7 cases per thousand. It had no effect on the cause of hemorrhage, but it reduced the blood loss in hemorrhages due to atony by as much as 16.5 per cent, and inasmuch as the average post-partum hemorrhage with an atonic uterus amounted to 1,060 c.cm., the saving was considerable.

5. The earlier administration of pituitary extract shortened the third stage of labor and caused 11 per cent more patients to terminate this stage within four minutes. This helped to increase the number of patients in the group having the lowest blood loss.

6. If the placenta is delivered within five minutes, prophylactic injection does not lessen the blood loss appreciably. However, when the third stage of labor lasts between six and ten minutes the blood loss is reduced 14 per cent, and when the placental stage requires more than ten minutes the blood loss is reduced 7.5 per cent. The average blood loss in these two groups was 250 and 380 c.cm., respec-

tively, and inasmuch as the percentage saved was inversely related to the amount of blood loss, the maximum saving did not amount to an ounce and a half.

7. The complications of the third stage of labor were about equally distributed in both series of cases.

The effective control of post-partum blood loss is the result of careful management of the third stage of labor, based on a thorough knowledge of the physiology and pathology involved. The prophylactic administration of solutions of the pituitary body is not productive of more disturbance, and appreciably reduces the blood loss in hemorrhages due to uterine atony only.

EDWARD L. CORNELL, M.D.

Baumann, T.: Investigations on the Vitamin-C Metabolism in Lactating Women and on the Grade of the Physiological and Pathological Vitamin-C Saturation of the Human Organism (Untersuchungen ueber den C-Vitaminstoffwechsel bei lactierenden Frauen und ueber den Grad der physiologischen und pathologischen C-Vitaminsaettigung des menschlichen Organismus). *Jahrb. f. Kinderh.*, 1937, 150: 193.

With a sufficient saturation with Vitamin C in lactating women, 50 per cent of the vitamin is excreted in the milk and urine after an administration of 100 mgm. of ascorbic acid. If the milk values of Vitamin C are about 3.5 or 4 mgm. per 100 c.cm., they indicate a well saturated organism. The milk content of Vitamin C stands in direct relationship to the Vitamin C concentration in the blood during the fasting state. Blood values below 0.8 or 1.0 mgm. per 100 c.cm. of ascorbic acid show a poorly saturated organism, whereas blood values above 1.4 mgm. per 100 c.cm. indicate a well saturated organism. In women in whom lactation is terminating the percentage of the Vitamin-C content increases, and the more saturated the organism, the greater the percentage becomes. With an increasing secretion of milk the percentage of the ascorbic-acid content does not diminish, and, therefore, the daily excretion of Vitamin C increases. There, is, therefore, in saturated lactating women, a parallelism between the amount of milk and the daily excretion of Vitamin C.

With a relative Vitamin-C deficiency of the organism these relationships are altered. There is a lower content of Vitamin C in the colostrum as an expression of the immaturity of the breast gland, without relationship to the Vitamin-A saturation of the particular woman.

The amount of Vitamin-C excretion in the urine depends upon the amount of the vitamin in the blood. Its excretion results only when the blood value is over 1 mgm. per 100 c.cm. This does not apply to the breast gland. Even with maximal saturation of the organism with Vitamin C, the Vitamin C concentration in the milk does not increase to more than from 7 to 8 mgm. per 100 c.cm. The lactating organism is capable of storing the Vitamin C. Twenty per cent of the amount of Vitamin C administered is used up by the lactating woman in her metabolism. With equal saturation and equal amounts of milk individual differences in the Vitamin-C concentration of the milk can be found.

The Vitamin-C requirement of lactating women is estimated at 50 mgm. per day. For wet nurses and the mothers of twins the requirement is correspondingly higher. The Vitamin-C content of human milk shows certain seasonal variations, with low values in November and December. The Vitamin-C requirement of infants lies between 8 and 17 mgm. per day. A single administration of Vitamin C is not sufficient for the determination of the degree of saturation; a more distinct picture is obtained with an additional administration of 100 mgm. per day. The physiological degree of saturation of the organism varies between wide limits and lies between a test dosage of from 0 to 40 mgm. per kilogram of body weight (the test dosage is the number of milligrams of ascorbic acid that must be administered until a distinct increase is demonstrable in the urine—(Widenbauer). Only with a test dosage of over 40 mgm. can a hypovitaminosis be spoken of. There is a parallelism between the fasting blood content of Vitamin C and the degree of Vitamin-C saturation of the organism. The physiological range lies between 0.4 and 2.45 mgm. per 100 c.cm. of blood. The disappearance of pathological phenomena by the administration of Vitamin C does not always depend upon the presence of a hypovitaminosis. Individual details should be read in the original.

(NEUWEILER). LOUIS NEUWELT, M.D.

GENITO-URINARY SURGERY

ADRENAL, KIDNEY, AND URETER

Cutler, H. H., Power, M. H., and Wilder, R. M.: Concentrations of Chloride, Sodium, and Potassium in the Urine and Blood: Their Diagnostic Significance in Adrenal Insufficiency. *J. Am. M. Ass.*, 1938, 111: 117.

Under standardized conditions the concentration of either chloride or sodium in the urine is more significant in the diagnosis of Addison's disease than is the volume of the urine, the concentration of potassium in the urine, or the values or change in values of the chloride, sodium, or potassium of the blood plasma. This conclusion is based on the examination of 17 patients suffering from Addison's disease and 37 controls, of whom 10 were healthy persons and 27 were patients suffering from diseases which apparently did not involve the adrenal glands.

The procedure for the diagnostic examination is as follows:

If the patient has been receiving either cortin or extra salts of sodium, these are withheld for a day before the examination. Throughout the examination the patient is given a diet that is low in salt, which contains 0.95 gm. of chloride ion, 0.59 gm. of sodium, and 4.1 gm. of potassium. On the first day the drinking of water is encouraged. On the afternoon of the first day 42 mgm. of potassium citrate per pound of body weight are given. On the second day the intake of liquid is made to equal 40 c.cm. per kilogram of the body weight. On the morning of the second day the dose of potassium citrate is repeated. On the third day 20 c.cm. of liquid per kilogram of body weight is given before 11 a.m. At noon of the third day the examination ends. At the close of the examination, all patients in whom adrenal insufficiency is suspected are given an intravenous injection of 1,000 c.cm. of sterile solution containing 50 gm. of *d*-glucose, 10 gm. of sodium chloride, 5 gm. of sodium citrate, and 20 c.cm. of an active preparation of cortical hormone. The constituents of this solution are held ready at all times for immediate use, if necessary. The concentration of chloride in the urine collected from 8 o'clock in the morning to 12, noon, of the third day is determined. A concentration in excess of 225 mgm. per cent indicates some abnormality of the adrenocortical function, whereas a concentration of less than 125 mgm. per cent can probably be accepted as evidence of normality. Concentrations between these two figures are inconclusive and a longer period of restricted intake of salt may be necessary for diagnosis.

Complicating organic disease, especially uncontrolled diabetes or some forms of nephritis, may make this test inapplicable for the diagnosis of Addison's disease. The examination of patients must not be undertaken unless rest in bed, or at least in the patient's room, is enforced, unless continuous nursing attention is provided, and unless facilities for the immediate intravenous injection of sodium chloride, sodium citrate, and cortical hormone are at hand in the event of emergency.

This test requires less time, subjects the patient to less risk of collapse, and, in most cases, is quite as informative as the six-day period of restricted intake of salt heretofore resorted to for diagnostic purposes. A further advantage is that the determination of concentration is a much simpler procedure for chloride than for sodium or potassium.

Walters, W., and Kepler, E. J.: Adrenal Cortical Tumors and Their Treatment. *Ann. Surg.*, 1938, 107: 881.

The histories of 7 consecutive patients from whom adrenal cortical tumors were removed at the Mayo Clinic between 1932 and 1937 are presented. All 7 patients showed in varying degrees the signs and symptoms known as the "adrenal cortical syndrome." The patients were all female and ranged in age from twenty-three months to thirty-nine years. All recovered from the operation. In 5 of the patients the removal of an encapsulated tumor produced prompt regression of the symptoms and there has been no recurrence of the tumor during periods of observation ranging from two months to five years. In the 2 other patients the carcinomatous tumor had penetrated the adrenal capsule and within a period of eighteen months after its removal it had recurred with fatal consequences.

Since most adrenal cortical tumors producing the syndrome are relatively malignant, but in the early stages are definitely encapsulated, it is important to make the diagnosis early and to remove the lesion before the cells have penetrated the capsule and invaded adjacent structures. The similarity of the clinical syndrome produced by an adrenal cortical tumor to pituitary basophilism may lead to the erroneous decision that the latter is present. In view of the facts: (1) that treatment of pituitary basophilism is entirely dependent on roentgen therapy, from which, in a very few cases, little more than palliative benefit has been obtained, (2) that adrenal cortical tumors are frequently the cause of a similar syndrome, and (3) that the removal of these tumors can usually be readily accomplished, Walters and Kepler believe that the adrenal gland should be explored if patients present this syndrome, provided that their condition permits.

Symptoms produced by an adrenal cortical tumor depend on the sex and age of the patient at the time the tumor begins to function. These tumors occur most often in women and produce variable changes in secondary sex characters, such as cessation of menstruation, occasional hypertrophy of the clitoris, and abnormal growth of hair with masculine dis-

tribution. Among girls, tumors of the adrenal cortex tend to produce precocious puberty, more masculine than feminine in character. The disease seldom occurs among males, either young or old. Other common symptoms are a florid complexion, purplish striations of the skin, acne, hypertension, diabetes (either clinical or latent), osteoporosis, weakness, and a gain in weight. Unfortunately for diagnostic purposes, there is much variation in the symptoms.

Hyperplasia of the adrenal cortex, which is sometimes associated with tumors of the thymus, may produce a clinical picture almost, if not entirely, identical with that seen in cases of pituitary basophilism or adrenal cortical tumor. Furthermore, masculinizing tumors of the ovaries (usually arrhenoblastoma, rarely granulosa-cell tumors) result in hirsutism of the male type, amenorrhea, and hypertrophy of the clitoris. However, such tumors practically never cause diabetes, hypertension, or osteoporosis. In children tumors or inflammation in the region of the pineal body may produce sexual and somatic precocity. Finally, many women have varying degrees of hirsutism, amenorrhea, hypertension, or obesity for which no adequate basis can be found. Since pituitary basophilism rarely occurs in children, the difficulty of differentiating it from an adrenal cortical tumor occurs chiefly in the cases of young women.

Routine laboratory studies have been of little aid in the differential diagnosis, although a high content of estrogenic substance in the urine suggests adrenal cortical carcinoma, provided that pregnancy is excluded. Injection of air about the adrenal gland has been of aid in localization of some adrenal tumors.

In 40 cases reported in the literature the surgical mortality rate was 47 per cent. In the opinion of Walters and Kepler the absence of mortality in the 7 consecutive cases which were operated upon at The Mayo Clinic is attributable to an increased understanding of the disturbance of physiological processes which follows removal of almost all hyperfunctioning tumors of the endocrine system and to an increased knowledge of the pathological physiology of Addison's disease; improved methods of treating acute adrenal insufficiency have thereby been developed. These consist primarily of the administration of large quantities of sodium chloride and sodium citrate, daily administration of an adequate amount of cortical hormone, and of a low potassium diet, throughout the postoperative period. The patient should be kept under the closest supervision not only during the first few hours after operation but until his complete recovery. Insufficiency of the adrenal cortex may at first be so mild in its clinical characteristics as to escape detection. Among the more important of the premonitory signs of acute adrenal failure are anorexia, hiccup, nausea, vomiting, weakness, insomnia, apathy, restlessness, an increasing pulse rate, and a falling blood pressure. Pyrexia accelerates the development of adrenal insufficiency and is therefore poorly tolerated. The clinical manifestations may precede any material change in the chemical composition of the blood. The blood pressure should be recorded every four hours and analyses of the blood for its content of sugar, chlorides, and urea should be made daily. If at any time the condition of the patient is in any way suggestive of adrenal insufficiency, more vigorous treatment should be instituted or treatment should be resumed if it has been discontinued. It is not generally appreciated that fatal adrenal failure can develop within a few hours. Danger lies in undertreatment rather than in overtreatment.

In the opinion of Walters and Kepler the surgical approach to the adrenal glands which gives the best opportunity for minute and careful inspection of the glands is through a posterolumbar incision similar to that used for exposure of the kidney. After the fascia of Gerota has been incised, the perirenal fat is reflected from the upper pole of the kidney and the kidney is retracted downward; this exposes the posterior aspect of the adrenal gland. In this way it can be studied accurately from every side without disturbance of the circulation; care is taken to prevent injury to the blood vessels which enter the adrenal gland on its mesial and inferior aspect.

Although Walters and Kepler have seen 1 case of minute multiple adenomas, in other cases adenomas have been recognized grossly with ease; they have varied from 2 to 15 cm. in diameter. When larger tumors are present practically the entire adrenal gland is thinned out and destroyed with the exception of a fringe a few millimeters long, which can be recognized by its brilliant yellow color as being adrenal cortical tissue. The right adrenal gland is in direct contact with the inferior vena cava. Usually the blood vessels supplying an adrenal tumor are much larger than those which supply the normal gland. On this account care must be taken to ligate them accurately.

GENITAL ORGANS

Wells, C. A.: Tuberculous Epididymitis. *Brit. J. Urol.*, 1938, 10: 114.

The author presents the subject of tuberculous epididymitis with the hope of proving that tuberculosis of the epididymis does not occur unless a primary focus of the genito-urinary tract is present in the kidney.

He quotes Medlar, Couland, Band, and others, and states that renal tuberculosis will heal. He bases his conclusions on the clinical findings of 55 cases of tuberculous epididymitis:

Of 32 personal patients with tuberculous epididymitis, 24 had destructive renal lesions; 3 had no evidence of a destructive lesion after full investigation; 1 had inconclusive evidence after a long period; 1 had evidence suggesting a healed lesion; and 3 were investigated with hopeless inadequacy.

Of the remaining 23 patients (i.e., not personal cases), 7 had frank renal lesions; 4 had good evidence of renal lesions, but the lesions were not diagnosed

as such; 2 were found to be free from kidney involvement after repeated investigations; 1 was traumatic in origin; and 9 were investigated with hopeless inadequacy.

The author discusses the route taken by the tuberculous bacilli in reaching the epididymis and considers the blood stream, the urinary stream, and the lymphatics. He contends that the kidney is involved through the blood stream because of a primary focus elsewhere in the body. The infection then descends to the bladder by the urinary stream and from the posterior urethra to the epididymis by way of the lumen of the vas. He further states that the lymphatics can definitely be excluded as a route of infection because of their distribution.

Relative to the blood stream's being the route by which the infection reaches the epididymis, the author makes the statement that "in blood stream infection as in mumps, etc., it is the body of the testicle and not the epididymis that is usually affected." Furthermore, the vascular supply to the testicle does not favor the constant selection of the epididymis. He further states that renal lesions heal, while the local infection of the epididymis may continue. The practical importance of this theory is that when a definite diagnosis of tuberculous epididymitis has been made, it is imperative that careful observation of the patient be made to determine the presence of destructive renal tuberculosis.

The author makes the following statements with regard to the care of patients with tuberculous epididymitis:

"1. Tuberculous epididymitis is a certain sign of renal tuberculosis and demands full and repeated renal investigation.

"2. The presence of tubercle bacilli even with blood and pus in the specimen segregated from one kidney does not damn that kidney out of hand. A destructive lesion must be demonstrated by pyelography before a diagnosis of surgical renal tuberculosis is justified.

"3. A demonstrable lesion never heals and a nephrectomy should be done.

"4. Back pressure changes caused by fibrosis of the bladder wall around the ureter of the healthier kidney may be misleading and may lead to an unwarranted diagnosis of bilateral disease.

"5. Nephro-ureterectomy is the operation of choice in cases in which the affected ureter is dilated due to obstruction at its lower end. These are the cases most likely to cause a persistent fistula.

"6. Epididymectomy is the operation of choice in tuberculous epididymitis. Carefully performed, it is a successful operation even in quite advanced cases with sinuses. It may, however, be impossible; e.g., the whole organ may have sloughed away. It is because of the risk of this occurrence as a sequel on the healthy side that epididymectomy is so important.

"7. The vas on the healthy side may be ligated and divided in certain circumstances. This operation prevents contra-lateral involvement and should be done, with the consent of the patient, (a) in old age, (b) when one testicle has been completely lost or needlessly sacrificed, and (c) in the presence of frank prostatitis and vesiculitis. It should not be done in young patients with a good general prognosis.

"8. In the absence of epididymitis, vasotomy is reasonable; e.g., one vas might be divided to protect one testicle and its fellow might be left to provide external secretion and take a risk! I should not, however, be prepared to advocate this measure.

"9. I have no experience of the radical excision of the vas and vesicle and have no reason to disagree with the opinion generally held in this country that it is an unnecessarily severe operation in the majority of cases." J. SYDNEY RITTER, M.D.

MISCELLANEOUS

Farrell, J. I.: The Secretion of Alcohol by the Genital Tract. *J. Urol.*, 1938, 40: 62.

The author has made a very careful study of the effect of alcohol on the genital organs of dogs.

The experimental data show that alcohol is eliminated by the prostate gland and, to a lesser extent, by the testicle. The motility of the sperm stops more quickly in alcoholic animals; the higher the concentration of the alcohol, the more quickly the motility of the sperm ceases. The concentration of the alcohol excreted by the prostate gland is very similar to that excreted in the urine. Since it has been shown that alcohol is deleterious to the diseased kidney, it would likewise appear to have a deleterious effect on the diseased prostate gland. The harmful action of alcohol in prostatic diseases, such as prostatitis and prostatic hypertrophy, is seen by all who have treated such diseases.

J. SYDNEY RITTER, M.D.

SURGERY OF THE BONES, JOINTS, MUSCLES, TENDONS

CONDITIONS OF THE BONES, JOINTS, MUSCLES, TENDONS, ETC.

De Langre and Cretin: Spontaneous Fracture in Osteomyelitis Simulating Sarcoma (Fracture spontanée par ostéomyélite simulant un sarcome). *Rev. d' orthop.*, 1938, 25: 320.

A case of osteomyelitis of the left femur which had been diagnosed as an osteosarcoma is presented from the clinical, medicolegal, and anatomical viewpoints.

Clinical. A forty-six-year-old man was sent to the hospital with the diagnosis of osteosarcoma of the left femur with spontaneous fracture. About five weeks previous the patient had twisted his left knee and had been confined to bed since the accident. His temperature had been within normal limits. There was a slight swelling on the lateral aspect of the thigh and knee.

When he entered the hospital, examination revealed considerable deformity of the thigh due to the fracture and a hard tumor with no signs of inflammation. The skin displayed a network of dilated veins over the tumor. The patient was quite anemic. The roentgenograms affirmed the presence of the tumor and fracture. The patient was prepared for operation, a biopsy of the tumor was taken, and no malignancy was found. Nevertheless, a disarticulation of the left hip was performed. The patient died very suddenly seven days following the operative procedure.

Medicolegal. The possibility that the acute osteomyelitis had been caused by the original accident must be considered. In this case the court affirmed that the accident aggravated the osteomyelitis which may have been present previously and which was responsible for the patient's present condition. Histological examination was in favor of an old infection. There is the possibility that an old osteomyelitis may be capable of remaining latent for months and even years. It would be impossible to state exactly what the evolution of that osteomyelitis may have been without the accident. The condition which possibly had already been present was aggravated and hastened the evolution of the fatal osteomyelitis. The legal accidental origin establishes the reality of the accident and the continuity of the troubles.

Anatomical. The bacteriological examination revealed definite peculiarities in this case of spontaneous fracture which differentiated it from cases of acute osteomyelitis. The staphylococcus pyogenes aureus was the offending organism.

Histological examination revealed that the femoral head and knee were entirely normal. Further examination showed a regular morphology indicative of reconstruction. Histochemically the albumins did not have the metachromatic character of young bone. There was no sequestration present as is seen in acute osteomyelitis.

RICHARD J. BENNETT, JR., M.D.

Larsen, R. M.: Intramedullary Pressure with Particular Reference to Massive Diaphyseal Bone Necrosis. *Ann. Surg.*, 1938, 108: 127.

This author suggests the hypothesis that massive necrosis of acute suppurative osteomyelitis may be due to ischemia caused by increased intramedullary pressure, the effect of which is enhanced by the rigidity of the walls of the medullary cavity and the close interdependence of volume blood flow and pressure which this anatomical characteristic implies. He presents several series of experimental studies of intramedullary pressure made with the use of a threaded steel cannula inserted into the medullary cavity. In normal dogs he finds that the relationship of arterial pressure to intramedullary pressure is approximately 3 to 1 and the intramedullary pressure changes parallel the changes in the arterial pressure. The intravenous injection of adrenalin produces a small rise in the intramedullary pressure simultaneous with an abrupt elevation of the arterial pressure, but the intramedullary pressure then drops precipitously and remains low during the period of elevation of the arterial pressure, gradually rising to its base level as the arterial pressure returns to normal. The injection of pituitrin causes a similar change. Ephedrine produces a prolonged increase in the intramedullary pressure, while histamine produces a small decrease. These results are what one would anticipate when dealing with a vascular network enclosed in rigid walls.

The author then describes a series of experiments in which elevation of the intramedullary pressure was produced by physiological saline solution. He found that pressures below 75 cm. of salt solution for from twenty-four to forty-eight hours do not lead to bone necrosis even in the presence of gross infection, but that medullary infusion of normal saline solution at pressures of 180 cm. or more for twelve hours or over produces massive bone necrosis, followed by massive sequestration in bones with unfused epiphyses and widespread resorption in bones with closed epiphyseal lines.

He concludes that increased intramedullary pressure may be of extreme importance in the production of massive bone necrosis, and suggests that sequestration of dead bone occurs only when there has been complete destruction and long-continued exclusion of the vascular connections between the bone and the surrounding vascular tissue. Therefore, the fundamental principle in the treatment of acute suppurative osteomyelitis is the early release of pressure in the infected bone before the bone is killed, in order to avoid massive necrosis and subsequent sequestration. DANIEL H. LEVINTHAL, M.D.

Dawson, E. K., Innes, J. R. M., and Harvey, W. F.: Debatable Tumors in Human and Animal Pathology. V. Giant-Cell Tumor of Bone. *J. Laryngol. & Otol.*, 1938, 53: 491.

The giant-cell tumor of bone is highly cellular, essentially an osteogenic tissue growth, characterized in its typically active form by the presence of numerous discrete multinucleated giant cells in the midst of much more numerous polyhedral or fusiform cells. The tumor may recur, but it so rarely develops into a malignancy with metastases that it may be regarded as practically benign.

Giant-cell tumor of bone is a neoplastic growth, probably originating with trauma and hemorrhage and developing as an osteogenic tissue reaction and proliferation, which may slowly progress and ultimately regress, but which, in rare cases, acquires the characteristics of an osteogenic sarcoma. It may be classed as a type of new growth intermediate between purely reactive tissue and true blastoma.

Trauma is an important causative agent of the growth of giant-cell tumors. These tumors are constantly associated with hemorrhage, which is followed by a characteristic neoplastic reaction of the osteogenic cellular tissues and vessels. This reaction is of a progressive nature, although it usually shows some regressive or reparative changes in the collagenous fibrocystic tissue in the form of cyst and bone formation, and in the disappearance of the multinucleated cells. The giant cells are produced by fusion of small primitive osteogenic tissue cells which are osteoclastic. An active giant-cell tumor of bone is a bone resorptive growth, but new osteoid bone is produced. This new bone is not wholly the result of a reaction of the periosteum which forms a crepitant capsule to the expanding tumor because bone is frequently found in the midst of the growth.

Regression means fibrosis, bone formation instead of bone absorption, and disappearance of the giant-cells, a histological picture which may give rise to errors in the diagnosis.

The diversity of views seems to be best unified if one regards the more primitive component cell types of the tumor as fibroblast, reticuloblast, angioblast, lipoblast, chondroblast, osteoblast and osteoclast, respectively, which proliferate continuously, though in a varying degree, and take origin in a mesenchymal cellular primordium. The prototype cell is the primitive pluripotential cell, with determination to a type of growth represented by fibropoiesis, angiopoiesis, lipopoiesis, chondropoiesis, osteopoiesis, and osteoclasis. The vascularity of these tumors is of a sinusoidal and cavernous type, and is analogous to that found in bone marrow.

A phase of the giant-cell tumor may initiate the ordinary osteogenic sarcoma but the change is rarely observed microscopically. Embryological mesenchymal and epithelial tissues persist as a residue in adult tissue. This residue tissue has all the potentialities of differentiation and is responsible for the production of granulation, reparative, and tumor tissues. The persistence of this *embryological* residue is greatest in the epiphyseal and metaphyseal regions, a fact which may explain the more frequent occurrence of solitary giant-cell tumor in adolescents and young adults in these locations.

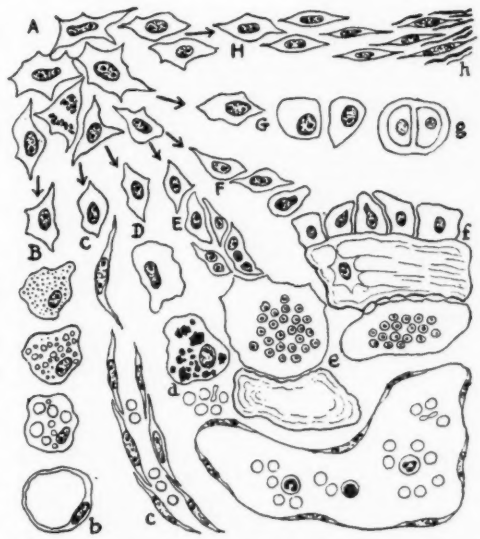

Fig. 1. Showing various stages of the "determination" of the primitive mesenchyme cells from which recognizable giant-cell tumor elements are derived. Primitive mesenchyme, A; lipoblast, B, to lipocyte, *b;* angioblast, C, to angiocyte (littoral endothelium), *c;* reticuloblast, D, to reticulocyte (macrophage), *d;* "pre-osteoclast," E, to osteoclast, *e,* absorbing bone; osteoblast, F, to osteocyte, *f,* forming bone; chondroblast, G, to chondrocyte, *g;* fibroblast, H, to fibrocyte, *h,* with collagen fibres. Hæmocytoblast to myeloid blood cells not indicated.

The giant-cell tumor of bone is regarded as a simple reaction and a true tumor of benign character. Interference or any other disturbing condition may be a factor in the development of greater cellularity and neoplastic activity, with ultimate malignancy and metastasis.

Specimens from 117 cases of bone tumor served as the basis of this report. Forty-five photomicrographs and explanatory captions are presented.

ROBERT P. MONTGOMERY, M.D.

Barr, J. S.: The Relationship of the Intervertebral Disc to Back Strain and Peripheral Pain (Sciatica). *Surgery*, 1938, 4: 1.

Intractable low back and sciatic pain is frequently due to the mechanical pressure of tissue of the intervertebral disc protruding posteriorly into the lumbar spinal canal and impinging on one or more roots of the cauda equina which go to form the lumbosacral plexus.

There are no physical, neurological, or orthopedic signs which are found only in cases of protrusion of

the intervertebral discs. All of the known signs may be found in other conditions. Yet, the symptoms and signs of a ruptured lumbar intervertebral disc are so constant and characteristic that a presumptive diagnosis can often be made before lipiodol roentgenographic studies are made.

Probably from 90 to 95 per cent of the patients who have sciatica recover either spontaneously or after conservative treatment and do not need to be subjected to the highly technical and possibly dangerous lipiodol examination.

It is only when sufficient disc material is displaced posteriorly into the canal to cause one or more roots of the cauda equina to be pinched that symptoms arise. Many patients with this lesion are relieved by conservative measures. The author has under observation a patient with a disc lesion, proved by lipiodol examination, who is perfectly comfortable if the spine is immobilized in a back brace or a plaster jacket, but who is incapacitated by severe pain if the support is removed. Unless there is evidence of neurological changes due to pressure on the nerve roots, adequate prolonged conservative treatment, such as is used for any back strain, should be insisted upon before a lipiodol examination is recommended. A ruptured intervertebral disc cannot be ruled out in any given case except by lipiodol roentgenographic study, done with the proper technique.

A ruptured intervertebral disc may cause sufficient pressure on the cauda equina to produce obvious paralysis and anesthesia, but the majority of these cases have protrusions so located and of such size that only one nerve root is pressed upon and the only symptom is referred pain, all objective neurological signs being absent. A negative neurological examination cannot be accepted as proof of the absence of this lesion. Also, it cannot be accepted that a given case is a "classical picture" of lumbosacral or sacro-iliac strain.

Arachnoiditis, characterized by matting together of the roots of the cauda equina, may cause intractable low back and sciatic pain, which is usually bilateral. Subarachnoid hemorrhage following trauma may produce the same symptoms. A lumbar puncture, if done in the area of fibrosis, will show the dynamic alterations of a complete or incomplete block, or it may be impossible to obtain fluid unless the needle is inserted at a higher level. The lipiodol examination is not characteristic, but an incomplete, very irregular slow filling or a block with an irregular margin is usually noted.

A thickened ligamentum flavum may constrict the dura and produce pressure on one or more roots of the cauda equina. Lipiodol examination usually reveals a constricted hour-glass type of filling defect on the posterior and lateral aspects of the spinal canal.

The "facet syndrome" and narrowing of the lumbosacral intervertebral interspace are conditions related to ruptured intervertebral discs. A ruptured intervertebral disc is not uncommonly the sequel to the trauma of lifting and to the ordinary wear and tear of every-day activity.

Laminectomy without removal of the protruding mass of disc tissue might relieve the symptoms by taking away one limb of the "nut-cracker" which is pinching the nerve root. Spine fusion, if done in a pain-free interval, might prevent the recurrence of symptoms and, indeed, has probably been done many times on unrecognized cases of lesions of the intervertebral disc. Laminectomy and removal of the ruptured, protruding portion of the disc is the logical treatment for this condition if conservative non-operative methods fail. The question of whether an attempt should be made to strengthen the spine by fusing the area of laminectomy is still unsettled. If the laminectomy leaves all articular facets intact, the spine is probably little weakened, but, if a facet is removed, fusion is indicated to prevent symptoms of a weak back. It is technically difficult to fuse a spine after laminectomy. The author has used a flexible osteoperiosteal tibial graft to bridge the osseous defect, has laid multiple bone chips over the graft, and has destroyed the articular facets by curettage. Nursing care is simplified if a plaster shell is made pre-operatively. The patient is allowed up with his back supported by a brace or a plaster jacket after six or eight weeks of recumbency. Heavy lifting should be avoided for six months.

The author presents a typical case history, examination, lumbar-puncture findings (a total protein higher than 35 or 40 mgm. to 100 c.cm. is confirmative evidence that the pathological process is intraspinal), and lipiodol examination. He also gives a table of signs, symptoms, and laboratory findings from 100 patients. There are also a second table showing the relationship between the anatomical pathology and the symptoms and signs, photographs of roentgenograms, and drawings of the operative exposure of a ruptured intervertebral disc.

ROBERT P. MONTGOMERY, M.D.

Rix, R. R., and Geschickter, C. F.: Tumors of the Spine, with a Consideration of Ewing's Sarcoma. *Arch. Surg.*, 1938, 36: 899.

Rix and Geschickter have carefully reviewed 291 tumors affecting the spinal column with special reference to the incidence of spinal tumors and to their pathological changes. All tumors were demonstrable roentgenologically.

Metastatic carcinoma, usually from the breast or prostate gland, was the most frequent neoplastic lesion of this series. Carcinoma of the breast showed no predilection for any part of the spine and usually produced multiple osteolytic lesions, although some were osteosclerotic. Carcinoma of the prostate gland involved the lumbar spine and sacrum, as a rule, and produced sclerosis of bone. The primary focus of the cancer in some cases remained undiscovered until the post-mortem examination. In other cases the primary lesion had been discovered and removed from ten to fourteen years prior to the occurrence of the spinal lesions.

The authors found that involvement of the spine in Hodgkin's disease, lymphosarcoma, and leucemia simulated metastatic carcinoma. These lesions were found to be rare in their series. They stressed that these multiple lesions of the spine in adults must be differentiated from multiple myeloma, which produces rarefied circular defects with a tendency toward pathological fracture and collapse.

Benign giant-cell tumors and osteochondromas were found to be the most common benign tumors of the spine. Giant-cell tumors affected the spine of young adults below the cervical spine, and tended to involve the neural arch and produce trabeculated lesions outside of the body of the vertebra. In spite of the fact that it is a benign tumor, 4 of the 14 patients died because of damage to the cord and invasion of the inferior vena cæva with resulting hemorrhage. The authors found 2 cases of atypical solitary cyst of the spine. They felt that the absence of typical bone cysts in association with tumors of the spinal column lent support to the opinion that bone cysts of long bones were the healing phase of giant-cell tumors. Multiple involvements of the spine, with bone atrophy and cyst formation occurred as a part of the syndrome of generalized osteitis fibrosa. There were 10 cases of osteochondroma which was found to involve any portion of the spine. Only 2 cases of hemangioma were found in this series, both producing the characteristic vertical striations. The rarity of this lesion is probably due to the fact that hemangiomas of the spine are not invasive and do not grow rapidly as a rule, and therefore they may be present in many cases without producing symptoms.

Malignant primary tumors were less common than benign growths. These included chondrosarcoma, osteolytic sarcoma, and sclerosing sarcoma. In several cases they were found to be secondary to multiple exostoses or Paget's disease. Chondrosarcoma occurred in all portions of the spine, tended to involve several vertebræ, and produced characteristic calcified paravertebral shadows. There were 8 cases of sarcoma, 4 osteolytic and 4 sclerosing types. The roentgenograms in the cases of the sclerosing type showed irregular formation of new bone in the soft parts. Osteolytic sarcomas were less characteristic and produced rapidly extending bony destruction, with infiltration of the soft parts. Chordomas were found in 5 cases. These involved either the spheno-occipital or the sacrococcygeal region of the spine of the adult and produced a slow-growing but malignant bone destructive lesion, which increased in size gradually over a period of months or years. This tumor kills by the invasion of vital structures.

Rix and Geschickter discuss 12 cases of undifferentiated neuroblastic tumors, sympathicoblastomas, involving the spine. These tumors usually involve the lower thoracic and lumbar spine, destroy bone, and produce a paravertebral shadow. They tend to metastasize to the regional lymph nodes and to other bones. They resemble the Ewing sarcoma microscopically and in its response to roentgen therapy. Both types also have similar staining qualities and metastasize to one or more bones, to the lungs, or to the lymph nodes. No typical Ewing sarcoma of the spine was found in the authors' series.

Glial or nerve-sheath tumors of the spinal cord were found to involve the vertebral column. Meningeal tumors occurred more frequently in the thoracic and cervical regions and were visible in roentgenograms either as erosive or calcified lesions. Neurinomas and neurofibromas of spinal nerve roots, however, more often caused erosion of bone than the meningeal tumors. The neurinomas were found more commonly in the lumbar and sacral regions.

DANIEL H. LEVINTHAL, M.D.

SURGERY OF THE BONES, JOINTS, MUSCLES, TENDONS, ETC.

Casuccio, C.: Post-Traumatic Cubitus Varus and Its Treatment (Cubito varo post-traumatico e suo trattamento). *Chir. d. organi di movimento*, 1938, 23: 460.

The normal valgus angle of the elbow is fixed by the author to be between 157 and 173 degrees, it being somewhat lower in the female than in the male.

It is doubtful whether or not a true congenital cubitus varus exists. Trauma is the most common cause, with such diseases as tuberculosis, tabes dorsalis, and arthritis playing a secondary rôle.

There is a very good bibliographical review plus a report of 7 personal cases from the Istituto Rizzoli of Bologna.

Of the 7 cases, 5 were treated by linear supracondylar osteotomy and 2 of these were followed by a recurrence of the deformity. In each of the remaining 2 cases a cuneiform osteotomy was done.

The author concluded that correction during the growing ages is followed by a high percentage of recurrences. The best results followed supracondylar cuneiform osteotomy. It is advisable to wait until the epiphyses have fused before the operation is performed. If this is not possible, repeated check-up with the roentgen-rays and exact measurements should be made and operation performed only when there is no longer an increase in the deformity.

CARLO SCUDERI, M.D.

Bunnell, S.: Opposition of the Thumb. *J. Bone & Joint Surg.*, 1938, 20: 269.

The term "opposition" implies opposite and far apart. The thumb to be in true opposition must not only be opposite the fingers and far forward from them but it must also be diametrically opposite to them by rotation, that is, with the pulp of the thumb facing the pulp of the fingers and with the thumb nail parallel to the palm.

The various parts of the act of opposing the thumb are described in detail.

The loss of opposition of the thumb results from loss of nerve function to the muscles of the radial half

of the thenar eminence, or loss of these muscles themselves, or it may be due to cicatricial contracture from infection which approximates the first two metacarpals, to adhesions which hold back the tendon of the extensor pollicis longus, or to flat-hand from faulty splinting or from ankylosis of the intercarpal and carpometacarpal joints. The act of opposition can often be restored if the causes are recognized and repaired.

When the nerve or thenar muscles are irreparable and mobilizing operations, if necessary, have been done, then tenoplasty by tendon grafting will restore good opposition if two major principles are followed. These principles are that the tendon must pull subcutaneously in the direction of the pisiform bone, and it must be inserted in the dorso-ulnar aspect of the base of the proximal phalanx of the thumb to give pronation. To make the tendon pull toward the pisiform bone, either a tendon pulley is constructed there or the tendon is looped around the distal part of the tendon of the flexor carpi ulnaris. It is important that the tendon does not pass under the transverse carpal ligament as this merely pulls the thumb into the palm. There are various muscles which can be used for motor power, such as the flexor carpi ulnaris, the palmaris longus, the flexor digitorum sublimis of the ring finger, or any long flexor muscle. The tendon of the extensor pollicis brevis is ideal to be drawn subcutaneously across the palm as it has the correct insertion into the dorso-ulnar portion of the thumb and can be attached to one of the tendons mentioned for motor power.

The article is supplied with photographs and illustrations of the principles involved.

HARVEY S. ALLEN, M.D.

Ober, F. R.: The Relation of the Fascia Lata to Mechanical Disabilities of the Spine. *Surgery*, 1938, 4: 21.

A detailed discussion of the mechanical relationship of the lower extremities to the trunk, and the effect of abnormal contractures of muscles and fasciæ of the lower extremities on the spine are presented.

Fascial contractures occur at the junction of the thigh and pelvis. Limitation in raising of the straight leg, forward flexion of the spine, prone knee flexion, or in extension and adduction at the hip joint is a sign by which fascial contractures at the junction of the thigh and pelvis can be demonstrated. Detailed descriptions of these signs and other tests are given.

When the iliotibial band is contracted all the anterior fascial connections are contracted and they produce flexion of the pelvis on the femur. The sacrum becomes more horizontal and the physiological curves of the spine are increased. In many cases of severe lame back of long duration, the persistent lumbar lordosis may be due to shortening of the interspinous ligaments and contractures of the lumbar fasciæ. A release of the contracted thigh fasciæ allows the lordosis to disappear rapidly and without symptoms in the mobile lumbar spine. In the "fixed" lordotic spine the curve disappears slowly and is attended by symptoms of low back strain as the result of irritation at the bony attachments of the lumbar fasciæ and interspinous ligaments from mechanical stretching.

Poor postures and lame backs are more promptly relieved if fascial contractures are disposed of early. The treatment of mechanical difficulties of the back, which are associated with fascia-lata contractures, consists of first removing or decreasing the contractures, and then securing a return of the spine to a normal physiological position. The deforming factors must be removed because the deformity increases the burden on the musculature that is trying to maintain a posture against a contracture.

The contractures may be relieved by conservative or operative methods, or a combination of both. Rest in bed, rest plus local immobilization, traction, fixation in a plaster spica, and physical therapy are employed in the treatment whenever indicated. Indications for specific conservative and operative therapy, and a description of the operative technique and postoperative care are given.

Indications for the operative relief of fascial contractures are meralgia paresthetica, sciatica of long standing, sciatica plus lame back, chronic lame back, unsuccessful lumbosacral fusion, and failure of fasciotomy on the opposite leg.

Operative treatment should be postponed until all other conservative measures have failed. Fasciotomy is a relatively simple operation, but its usefulness is limited to a selected group of cases.

There is a definite relationship between lame backs and sciatica in some cases. The author emphasizes, however, that it must not be assumed that contracted fasciæ are responsible for all cases of lame back and sciatica, and that a proper diagnosis must be made before the fascia-lata and iliotibial bands are divided. ROBERT P. MONTGOMERY, M.D.

SURGERY OF THE BLOOD AND LYMPH SYSTEMS

BLOOD VESSELS

Laubry, C., and Louvel, J.: Stokes' Law in Venous Pathology (La loi de Stokes en pathologie veineuse). *Presse méd.*, Par., 1938, 46: 505.

According to Stokes' law inflammation of a serous membrane produces paralysis of the adjacent muscle. This law has been applied particularly to the intestinal tract, but Laubry and Louvel maintain that it can also be applied to the venous system. There is a close resemblance between the structure of the intestinal and that of the venous walls. Recent studies have shown that the outer coat of the veins is, in fact, a serous membrane. If this is so, pathological changes in this serous coat should cause a paralytic inhibition of the function of the muscular coat according to Stokes' law. Actual pathological conditions confirm this logical deduction. In particular the authors discuss subacute and chronic periphlebitis, venous changes in gout, and hemorrhoidal rectitis.

In recurrent attacks of periphlebitis, the initial attacks are characterized by inflammation of the outer tunic of the veins and of the neighboring tissues. There is an enlargement of the affected veins, due to loss of tonus of the muscularis, but as the inflammation subsides, the muscularis regains its tonicity, and the veins become normal in size. It is only when attacks have recurred repeatedly, that the return of muscular tonus is not complete and the veins become permanently dilated. In the earlier stages, the pathological changes in the venous walls follow the Stokes' law.

In attacks of gout, the outer coat of the veins in the region affected is involved, as gout characteristically attacks serous membranes primarily. This results in dilatation and loss of tone of these vessels, which is one of the characteristic symptoms of gout. This condition subsides with the acute attack, showing that the dilatation and atony of the veins are due to the temporary paralysis of the muscularis resulting, according to Stokes' law, from the inflammation of the outer coat.

Hemorrhoids are associated with inflammation of the mucosa and submucosa of the rectum, and in the opinion of the authors, this inflammation is the primary condition, inflammation of the outer coat of the veins being secondary. In accordance with Stokes' law, the inflammation of the outer coat of the vein results in atony of the muscularis, with hemorrhoidal dilatation. ALICE M. MEYERS.

Kaplan, T.: Thrombosis of the Axillary Vein: Report of 5 Cases, with Comments on Etiology, Pathology, and Diagnosis. *J. Am. M. Ass.*, 1938, 110: 2059.

The author notes that, although thrombosis of veins is common in the pelvic region and in the lower extremities, in the veins of the upper extremities it is not common. Thrombosis of the axillary vein caused by trauma from effort is comparatively rare. An extensive review of the literature is presented. Five cases of thrombosis of the axillary vein in males were observed by the author and the report of his findings is given in detail.

The theory is advanced that as a result of sudden stretching and compression of the axillary vein, localized phlebitis follows, which in turn leads to thrombosis within the vein. By dissection, Lowenstein observed that, with the arm in the abducted position, the costocoracoid ligament and subclavius muscle indented the axillary vein. When the arm is held in abduction or extension, the axillary vein is distended. Some contend that with distention of the axillary vein, pressure made by the costocoracoid ligament and subclavius muscle is sufficient to cause thrombosis. Other observers, on the basis of roentgen and autopsy studies, are of the opinion that the constriction of the vein occurs below the head of the humerus and against the subscapularis muscle. In violent trauma to the vein, a valve may be ruptured, which, in the opinion of other writers, is the fundamental basis of the thrombus. These theories do not explain those cases in which trauma is slight, or those occasional spontaneous cases without any history of injury. Reference is made to the findings of Cottalorda who, on operation, found no thrombosis but discovered that the vein was in a state of spasm. He advanced the theory that the lesion need not necessarily consist of a thrombus formation but that the vein may be held in a spastic state as a result of the irritation of the perisympathetic venous plexus.

Prognosis as to life is good and duration of the disability is variable. Patients may be completely restored in from one to two months but in many cases the convalescence is prolonged because of edema, weakness, and stiffness of the arm.

In the acute stage the treatment consists of rest, elevation, and hot moist packs applied locally. For residual edema, an elastic bandage may be applied, beginning at the hand and extending upward to the shoulder. The advisability of removal of the thrombus by excision is questionable, since after removal recurrence is likely.

The diagnosis of primary axillary thrombosis is made on the basis of characteristic symptoms and signs. An important symptom is swelling of the arm with cyanosis that occurs within several hours or even days after the accident. There may be a history of an injury by strain. Occasionally no history of injury is given. Dilated, superficial veins are seen on the affected arm and over the anterior part of the chest and in the axilla. There is no fever and there are no signs of local active inflammation. The venous pressure in the affected extremity is increased and the circulation time prolonged. When the arm is

raised above the heart level, there is a delay or absence in the collapse of its superficial veins.

Roentgen examination with radiopaque dyes injected into the vein of the affected arm reveals the new collateral formation with enlargement and dilatation of the veins. In primary axillary thrombosis, the axillary vein is not visualized by this technique. HERBERT F. THURSTON, M.D.

Andersson, O.: Venography in a Case of So-Called Traumatic Thrombosis of the Axillary Vein. *Acta radiol.*, 1938, 19: 126.

In the preliminary historical note, the author observes that the peripheral vascular system is not accessible to direct investigation by roentgenography except in cases with calcification of the vessel walls. Attempts were made to fill the blood vessels with opaque material, but the difficulty lay in finding a suitable contrast medium. Bismuth oil and lipiodol were eliminated clinically because of the danger of fatal embolism. Some halogen derivatives, such as sodium iodide, are not free from danger for they may injure the intimal coat of the vessels. When the iodine complex is organically combined, as in uroselectan, little or no irritating effect may result. Colloidal solutions, such as thorotrast, are utilized without giving rise to irritating effects on the injected vessel. It is not yet definitely known whether these latter media are entirely without injurious consequences.

Arteriography has been employed in encephalography, for the localization of emboli, for example. Venography has remained more in the background and has not yet arrived at the stage of actual clinical applicability. Dahl made use of venography to evaluate the speed of the venous current in his postoperative roentgen studies. This method of visualization of veins has been used in some cases of so-called traumatic thrombosis of the axillary vein. The author reports his experience with venography in a case of traumatic thrombosis of the axillary vein.

The technique is simple and resembles an ordinary intravenous injection into a cubital vein with the patient recumbent and the arm slightly abducted. Usually, 3 or 4 c.cm. of the contrast medium are required. An exposure, which reveals the injected vessel filled up as far as the axillary vein, is taken during the injection or exactly at its completion. The contrast effect disappears, usually at the level of the clavicle, because of the inflow of blood from so many large veins with the consequent dilution of the medium. To obtain the best possible filling of the axillary vein, the injection should be made into the basilic or into the median cubital vein.

Obstruction in the venous drainage of an extremity may be due to thrombosis or to compression of the vessel by tumors, lymph nodes, or masses of callus. In such cases, venography may provide information as to the venous drainage through collaterals, if not in respect to the site of obstruction. A fresh thrombosis should be regarded as a contraindication for venography on account of the hazard of embolism.

So-called traumatic thrombosis of the axillary vein is rare and the clinical findings are quite characteristic. The symptoms begin with a rapidly developing stasis and swelling of the arm. Cyanosis gradually develops with distention of the cutaneous veins and of those of the pectoral area. The subjective symptoms are a feeling of tiredness and weight in the arm, sometimes even gentle pains. There is often slight tenderness where the vein may be palpated as a firm cord. In most instances the patients are young, healthy individuals, usually men, and generally of strong muscular types. In 80 per cent of the patients reported, the symptoms are confined to the right arm. By conservative treatment with rest and the application of heat, the symptoms usually recede in the course of one or two months.

The etiology is not clear and a number of theories have been advanced in the literature. All investigators are agreed, however, that the exciting factor is trauma. There must be a primary factor, however, for trauma can only activate the symptoms. The condition has been interpreted as a genuine thrombosis, probably due to intimal injury of some sort. Some observers assume the presence of overextension of the veins in connection with overexertion, while others have suggested a compression of the veins by fascial and muscular fibers. Certain French writers have assumed a venospasm due to traumatic irritation of the sympathetic nervous system.

The author presents a case from St. Erik's Hospital, that of a woman twenty-six years of age, who had previously been in good health. She worked in a library and after putting books on shelves, in the course of a few weeks, noticed a swelling and sense of weight in the left arm, as well as prominence of the superficial vessels of the upper arm and axillary region. Upon her admittance to the hospital, venography with contrast material revealed a well developed collateral vein along the lateral thoracic wall with obstruction in the axillary vein. The nature of this obstruction was not definite. A venogram of the right arm revealed normal conditions. With conservative treatment the swelling decreased and a month after the patient's discharge from the hospital, a new venogram revealed filling of the collateral vessels, indicating the persistence of an obstruction to drainage in the axillary vein.

In conclusion, the author stresses the value of venography as an auxiliary to diagnosis in conditions with evidence of venous obstruction in the upper extremities. The method may provide information as to the collateral circulation and sometimes even as to the site and type of obstruction. In his opinion, the procedure is contra-indicated in fresh cases of genuine thrombosis.

HERBERT F. THURSTON, M.D.

SURGICAL TECHNIQUE

OPERATIVE SURGERY AND TECHNIQUE; POSTOPERATIVE TREATMENT

Hart, D.: Sterilization of the Air in the Operating Room with Bactericidal Radiation. Comparative Analysis of 132 Individual Stages of Extrapleural Thoracoplasties Performed with Radiation and 110 Stages Performed Without Radiation. *J. Thoracic Surg.*, 1938, 7: 525.

Hart contrasts the incidence of wound infections in 132 individual stages of thoracoplasties during the last fifteen months, when irradiation of the operative field was employed, with a series of 110 similar procedures performed in the six years before ultraviolet irradiation was instituted. In the irradiated series there were no deaths from infection, and the incidence of infection was only 3.8 per cent, while in the earlier series there were 4 deaths from infection, or 3.6 per cent, and the incidence of infection was 33 per cent. Hart believes that this improvement is attributable to the use of ultraviolet irradiation, of both the operative field and the air of the operating room, which brings about a marked reduction in the number of organisms introduced into the wounds. He also points out that the temperature elevations were less high and less prolonged in cases operated upon with the new technique than with the old; that healing was more rapid in the irradiated group; that drainage was unnecessary; and that the interval between stages could safely be reduced if ultraviolet irradiation was used.

In his conclusion he emphasizes the importance of atraumatic technique and meticulous hemostasis, with the free use of silk, in the decrease of the incidence of infection. However, conditions are not ideal in thoracoplasty operations, and any measure which reduces the number of organisms gaining entrance to the field will be particularly helpful in this type of surgery. Another improvement in technique is the employment of subcuticular sutures of wire for wounds which later will have to be reopened. This decreases the number of organisms entering the subcutaneous tissue from the skin. The author does not comment on the possibility that an important factor in the reduction of infections might have been the improvements in technique made possible by the greater number of patients treated per year during the period when irradiation was used, than the number treated during the preceding years. JOHN S. LOCKWOOD, M.D.

Riese, J.: The Hematoma-Phobia and the Prevention of Hematomas (Haematomfurcht und Haematomverhuetung). *Zentralbl. f. Chir.*, 1938, p. 1059.

This article is opposed to the assertions of Noetzel, who stated that the prevention of hematoma is the duty of every conscientious physician and emphasized this statement in opposition to the proposal, bobbing up frequently of late, that subcutaneous ligatures be avoided. Riese expresses the opinion, based on his earlier works, that the statement that the formation of hematoma favors suppuration is not correct. On the other hand, it was proved that tissue-necrosis results from ligation, or, at the crushed places, from application of the artery forceps and leads more readily to suppurative processes. It is true that when the author began to reduce the ligation of the bleeding vessels to the lowest possible point, the number of hematomas increased at once from 4.5 to 5.5 per cent. Now, however, he has fewer hematomas than previously. When hematomas develop as a result of coughing or vomiting, they are invariably found to be sterile. Nevertheless they should be avoided, not so much because they favor suppuration, as because they hinder direct apposition of the wound surfaces and delay healing thereby, and because there is the danger of their breaking through and becoming secondarily infected. When a hematoma develops the author waits until the ninth or tenth day before he removes the stitches. Small effusions of blood are punctured aside from the suture line; large ones are opened within the first twelve or twenty-four hours, as a rule, and the bleeding vessel is ligated (it is always only one vessel that is bleeding) and immediately sutured secondarily. Invariably there is primary healing. When a wound breaks open later and a hematoma breaks through, it is removed, and the edges of the wound are freshened and resutured immediately. In these cases the healing is also by first intention. With regard to the formation of hematomas, the author refers to his experiences with the much-feared scrotal hematoma. Previously, when ligation was always carefully carried out, the complication was more frequent; now it is a rarity. He avoids all compressive dressings and the laying on of sand-bags, since the normal circulation of the blood and nourishment of the tissues are disturbed thereby, and secondary bleeding occurs.

When operating Riese is governed by the following rules:

1. Bleeding from skin, fat, and muscle vessels is disregarded. If the bleeding obscures the field of operation it is packed off.

2. Sponging and wiping with gauze, immediately preceding the suturing of the wound, are entirely avoided, since by these means an impetus to secondary bleeding is given and spontaneous hemostasis is hindered. Coagula and fat-particles are carefully removed with a pincette.

3. Vessels which are still bleeding when the skin is to be sutured (a great rarity) are ligated.

4. Only the peritoneum, fascia, and skin are sutured. The stitches are placed close together but they are drawn loosely.

5. Compressive dressings as well as sand-bags are never used. Riese has never encountered severe secondary hemorrhage, nor has Boehler in 15,000 accidental wounds.

Riese also believes that, contrary to the views of Schmieden and Gorgon, we shall come closer to the avoidance of postoperative suppuration in aseptic operations as we practice operating in silence, lose our fear of the development of hematoma, and ligate as little as possible. The universal statistical average of 7.4 per cent suppuration has been lowered by Riese to 0.095 per cent since he introduced his method of silent operating, and his cases of hematoma are much fewer than previously when he was stopping the bleeding at once with forceps or ligation. (Franz). John W. Brennan, M.D.

Kaunitz, J.: Dry and Wet Stages of Obstructive Atelectasis. *J. Thoracic Surg.*, 1938, 7: 512.

Although the term atelectasis has been subject to much criticism and in its true sense may be best applied to the congenital state in which the lung is airless or collapsed, it seems proper to use it to the exclusion of all others in the airless condition resulting from bronchial obstruction. The term, however, fails to suggest the mechanisms of development of the process, its etiology, or its sequelæ. The simple condition, too, is rarely found in long-standing cases of bronchial obstruction as there is subsequent pneumonic consolidation, abscess formation, bronchiectasis, or fibrosis.

Atelectasis may be massive, lobar, or lobular, the type depending upon the bronchus occluded. In acute conditions, especially following surgery, an entire lung may be involved, while, in the aged or in invalids kept for long intervals in the decubitus position, stasis of the mucus in the smaller bronchi may result in patch or lobular atelectasis. The author wishes to stress three arbitrary stages of atelectasis as the result of bronchial obstruction: (1) the dry or early stage which occurs with the absorption of alveolar gases; (2) the wet stage resulting from the transudation of plasma and the accumulation of bronchial secretions in the alveoli; and (3) the fibrotic stage which follows a wet stage and denudation of the alveolar epithelium.

The roentgenographic shadows of the obstructive atelectasis differ in accordance with the stage. The clinical diagnosis of atelectasis is discussed in this article and the differential points in the three stages are stressed and well illustrated.

Howard B. Carroll, M.D.

ANTISEPTIC SURGERY; TREATMENT OF WOUNDS AND INFECTIONS

Blair, V. P., and Byars, L. T.: The Treatment of Wounds Resulting from Deep Burns. *J. Am. M. Ass.*, 1938, 110: 1802.

On the average, deep burns constitute the most neglected of all wounds amenable to surgery. Because of this, hospitalization and the wound-dressing period are unnecessarily prolonged and often followed by months, years, or possibly a lifetime of discomfort or disability, pending a belated surgical repair. This statement is based on a series of 340 late burns, treated since 1918, in which the average time that elapsed between injury and inauguration of surgical repair was five and one-tenth years. The average period of disability in this group from the time of injury until final discharge was six and eight-tenths years.

During the first several weeks after the infliction of the injury it is unnecessary and often impossible to distinguish between partial and full-thickness destruction of the skin, but areas of both types of destruction are commonly present in almost every extensive burn. The primary consideration during this early period is the immediate problem of saving life. The greatest help will come from the control of pain, worry, and infection. This most critical time having been successfully bridged, active steps for surgical repair are in order. Our observation of the cases cited forced the conclusion that opportunities for early repair had not been adequately met in the great majority of instances, because of the lack of realization either that what was a burn had changed to a granulating wound, or that the closure of this residual wound could be materially hastened by appropriate surgical attention. After total destruction of the skin, spontaneous repair is of late occurrence and is accomplished by three distinct but somewhat overlapping processes. First, the raw surface is gradually covered by granulations; second, the deeper and older layer of these granulations takes on the character of a contracting scar which draws in the surrounding skin and superficial fascia and thus decreases the actual surface area to be repaired; third, after some days, weeks, or months, earlier under proper treatment, epithelization of the remaining raw surface starts with a visible ingrowth of the surrounding skin.

Examples of raw surfaces which have persisted for from three to thirteen years or more after a burn are not lacking in our series. In contradistinction to the second-degree burn, the time at which surgical repair of extensive third-degree burns can be advantageously undertaken will in most cases be very largely influenced by the type of local and general care that was administered from the time the burn occurred.

The great majority of surface burns do not quite destroy the full thickness of the skin, and healing will therefore occur spontaneously in what appears to be a reasonable time, regardless of the type of treatment used. However, when any plan of expectant treatment is relied on entirely in the care of the less frequently occurring large deep burn, the result may be unfortunate for the patient.

Active surgical repair of a deep burn of any considerable size should be initiated as early as is practicable in the healing period, and permanent skin coverage of all raw surfaces should be performed in one or several operative steps. This may be ac-

complished completely by the application of large split grafts, or partially with scattered small grafts that serve as foci from which epithelization spreads in all directions; it should be done with the least possible disturbance to an already sick patient. Usually the patient can be put in a fair condition before this is attempted, but sometimes very simple types of grafting are done in the hope of aiding a patient who is making poor headway. When grafts are applied to an extensive raw surface at this early period, no special attempt is made to correct contractions that have already occurred, but a successful take should greatly limit further distortion and permit the healing period to be measured in terms of days rather than of weeks, months, or even years.

The chief factors in the late correction are the liberation of false union and the elimination of binding scars. These can usually be done by the excision of scar areas down to their deepest elastic layer, and by the immediate application of large split-thickness skin grafts, full-thickness grafts, or a sliding or pedicled flap. There is little to be gained by the attempt to grow skin grafts on a granulating area of years' duration without first the removal of the granulations, as well as of the underlying scar, which may be from a fourth to a half of an inch thick. Most important of all is the proper early care and coverage of deep burns of the back of the hand and fingers, where the tendons and joint capsules lie almost immediately beneath the skin. Few hands that have been allowed to heal spontaneously (having remained uncovered for months or having been allowed to rest out of the position of function) can ever be restored to anything like normal usefulness.

Abel, J. J., Hampil, B., Jonas, A. F., and Chalian, W.: Researches on Tetanus. VII. (1) The Time Required for the Fixation of a Fatal Quantity of Tetanus Toxin: (2) the Return Passage of Toxin by Way of the Lymphatic Capillaries to the Cardiovascular System; (3) the Return Passage as the Basis of a Method for the Approximate Determination of the Volume of Lymph in the Closed Lymphatic System. *Bull. Johns Hopkins Hosp.*, Balt., 1938, 62: 522.

On the basis of animal experiments, the details of which are recited in the paper, the authors arrive at the following conclusions:

When an animal has been injected with one or more lethal doses of tetanus toxin, the time of its death is determined by that fraction of the toxin that has been fixed by the specifically reacting organs of the body in the first few hours during which they were exposed to the requisite threshold concentration of the poison. Neither the bio-assay nor any other method now at our disposal enables us to detect and assay this fixed fraction of injected toxin.

When three lethal doses of the toxin were injected intravenously, the irreversible fixation of a lethal dose was completed in the relatively short time of from five to seven hours. This and the other facts enumerated below were established with the help of the "wash-out" method.

The toxin begins to be fixed in an irreversible manner from the moment it reaches, via the blood stream, the motor neurons of the central nervous system and the end-plates of the voluntary muscles. There is no brain-blood barrier that stands in the way of the steadily progressing uptake and fixation of blood-borne toxin by central motor neurons.

When a dog is given time to fix a lethal fraction of several intravenously injected dog lethal doses, and is then deprived of the free circulating toxin by the method of viviperfusion with whole blood, the injection of a relatively large dose of antitoxin during the period of incubation will save the animal. The antitoxin saves life under these conditions by neutralizing the toxin that has been irreversibly fixed by the motor neurons and the motor end-plates. The long-held belief that an impenetrable brain-blood barrier stands in the way of the uptake of blood-borne tetanus antitoxin is therefore just as untenable as is the belief that blood-borne tetanus toxin is unable, by its diffusive power, to pass through this assumedly impenetrable barrier. After a single truly lethal dose of the toxin, or after many lethal doses have once been fixed, the prophylactic action of the largest possible amounts of anti-tetanic serum that can be injected will not save the animal if the injection of the serum is delayed until the first symptoms of a descending tetanus are clearly in evidence.

It must not, however, be thought that a conclusion of this kind, which is based upon animal experiments in which all of the several factors that determine death are completely under control, is directly applicable to human tetanus. In dealing with a case of general tetanus in man, in which none of the factors is under control, and in which there is now no way of learning whether a full lethal dose of the toxin, or less, has already been fixed in the body, no other course is open to the physician than to inject anti-tetanic serum in accordance with present usage.

Within eight hours after the intravenous injection of many lethal doses, an equipartition, in the sense that the blood and the lymph of the thoracic duct contain the same amount of toxin per cubic centimeter, is established between the two fluids.

The reverse passage of the toxin that occurs in the course of the "wash-out" or viviperfusion experiments gives us a method of approximately determining the lymph volume of the closed lymphatic system of a normal resting animal.

HAROLD OCHSNER, M.D.

Starup, U.: Review of the Newer Experiences with Prontosil and Related Substances (Eine Uebersicht ueber die neueren Erfahrungen mit Prontosil und verwandten Substanzen). *Hosp.-Tid.*, 1937, p. 1232.

The treatment with prontosil of infections with pathogenic cocci has shown extremely favorable results. It has been the same with the various combinations related to prontosil. Prontosil is a red azodyestuff, 4-sulphonamid-2-4-diamino-azobenzol. It

is easily and quickly absorbed by the intestine and pharmacologically extraordinarily indifferent. It is administered per-orally, subcutaneously, and intravenously, and is rapidly excreted through the kidneys. In the streptococcus sepsis of the mouse and rabbit it exerts a selective streptococcus-bactericidal effect. *In vitro*, on the contrary, it is but meagerly bactericidal. Soluble prontosil, which was produced later, has a corresponding therapeutic effect, and, because of its solubility, is better adapted to injection-treatments than prontosil, to which preparation it is, even chemically, but distantly related: di-sodium salt of 4-sulphonamidophenylazo-7-acethylamino-1-oxynaphthalin-3-6-di-sulphonic acid. Other bactericidal preparations which are cited are prontosil album, prontylin, and colsulamyd, all of which may be included under the one general name, sulfanilamide. The effectiveness of the prontosils may reside in the splitting off of sulfanilamide components in the living organism. Sulfanilamide therapy seems to have special efficacy in the following streptococcic infections: puerperal fever, infected abortions, severe anginas; in these cases the treatment, without a doubt, results in a decrease in the number of fatalities. Good results are also observed in the treatment of erysipelas, however, not of its complications, which remain unchanged in incidence as well as severity. Up to the present time the treatment of septic conditions with pyemic complications in the organs has remained without positive results. This is true also of the treatment of endocarditis. The sulfanilamide combinations seem to be without significance as a means of the treatment of staphylococcus infections, although good results have been reported in a few instances. Favorable effects have been observed also following intralumbal and peroral administration in cases of meningitis. Likewise, in cases of gonococcus infection, a few favorable experiences have been reported. Sulfanilamide has been employed extensively in the treatment of infections of the urinary tract, especially in children. In these cases good results have been attained in the colon-bacillus, as well as in the coccal infections, the good effects appearing rapidly in these cases. Results seem to be superior to those of mandelic-acid therapy.

As a rule soluble prontosil is injected in daily doses of from 20 to 40 c.cm. and more, and sulfanilamide in daily oral doses of from 2 to 4 gm. The toxic dose of this preparation seems to be a very high one. The blood pressure and cardiac function are unaffected. Even in cases of kidney disease the kidney function remains uninfluenced. At the most, in administration by mouth, dyspeptic symptoms, and in high dosage, elevation of the body temperature develop, which may be accompanied by exanthema. However, neither swelling of the glands nor joint pains accompany these manifestations, which tend to disappear after from four to ten days. Among the only recently recognized complications may be included severe anemias and simple agranulocytosis. However, in spite of the extraordinarily large number of cases treated, these complications are observed only as an occasional phenomenon, explainable as a stray instance of sulfanilamide intolerance. The author refers to a complication of the nervous system observed by Bucy: in a patient who had received treatment with sulfanilamide for a recurring osteomyelitis, a toxic optic neuritis developed.

In consideration, therefore, of the cited complications and despite its excellent therapeutic effectiveness, sulfanilamide should be used only under the strictest indications and close watching.

(Haagen). John W. Brennan, M.D.

ANESTHESIA

Macdonald, A. D., and Watkins, K. H.: An Experimental Investigation into the Cause of Paralysis Following Spinal Anesthesia. *Brit. J. Surg.*, 1938, 25: 879.

The authors used cats in their experimental investigation into the cause of paralysis following spinal anesthesia. Heavy durocaine, in the same concentration but in greater bulk than when used for spinal anesthesia in man, was injected intrathecally. They also injected separately the various constituents of the anesthetic solution, without the addition of the active ingredient, procaine. A total of 150 cats were studied. In 23 of these, injected with alcohol and glycerine alone, there was no evidence of development of a cauda-equina syndrome (urinary incontinence, fecal incontinence, loss of reflexes, paralysis of hind limbs and tail). In an equal number of cats injected with heavy durocaine, 56 per cent became paralyzed.

In studying the relationship of the dosage of procaine HCl to the incidence of the symptoms, the authors found that in 20 cats injected with a 2.5 per cent concentration, no paralysis occurred; of 20 cats injected with a 5 per cent concentration, 10 per cent became paralyzed; of 56 cats injected with a 10 per cent concentration, 43 per cent were paralyzed; and of 8 cats injected with a 20 per cent concentration, 80 per cent were paralyzed and 3 of the 8 died. It should be recalled that from 2 to 3 c.cm. of from 7 to 10 per cent durocaine is usually used in man.

The heavy durocaine which was used by the authors was of the following composition:

Procaine HCl, "Planocaine" brand	0.1	gm. per c.cm.
Gliadin	0.00325	gm. per c.cm.
Glycerine	0.1	gm. per c.cm.

This was altered to the following composition:

Procaine HCl, "Planocaine" brand	0.1	gm. per c.cm.
Gum acacia	0.002	gm. per c.cm.
Glycerine	0.0416	gm. per c.cm.

In both cases the solutions were made up in 15 per cent ethyl alcohol. John Martin, M.D.

Ferguson, F. R., and Watkins, K. H.: Paralysis of the Bladder and Associated Neurological Sequelæ of Spinal Anesthesia (Cauda-Equina Syndrome). *Brit. J. Surg.*, 1938, 25: 735.

Impressed by the consistency of the symptoms in the so-called "cauda equina syndrome," Ferguson and Watkins, of the Manchester Royal Infirmary, report upon 14 cases of spinal anesthesia with resultant neurological dysfunction. Before their report, only 16 examples of this same condition were to be found in the literature.

It is not their purpose to disparage spinal anesthesia, which they look upon as a logical and valuable procedure; but they believe that the untoward results, when they occur, are so distressing that it seems important to study the mechanism of the production of the caudal pathology. In the authors' cases, almost immediately following spinal anesthesia, there were: (1) retention of urine, succeeded by incontinence; (2) incontinence of feces, with variable degrees of loss of sphincter tone in various individuals; (3) impairment of sensation in the saddle area, in some cases extending down the posterior surface of one thigh; and (4) absence or diminution of one ankle reflex, and occasionally absence of both ankle reflexes and even of the knee reflexes. The patients formed a group so striking as to the similarity of their symptoms that it was believed that a definite type of cauda-equina lesion must have been produced in some manner by the spinal anesthetic. Heavy duracaine had been used in all cases. The bladder symptoms were immediate, but the rectal symptoms were delayed up to ten days, which suggested, perhaps, a progressive lesion. The bladders showed a retention of the urine and a large capacity; some of them showed marked trabeculation of the walls, and nocturnal incontinence; frequency was common. The anal tone gradually recovered in from one and one-half to thirty-two months, but in some cases there was a very troublesome rectal anesthesia. Saddle anesthesia (sacral 3, 4, and 5) was a general complaint; it had been present for at least one year in all patients, and in some patients as long as three years. The loss of the deep tendon reflexes varied rather widely in degree. Some patients showed marked motor involvement, and all 14 patients presented some amount of weakness, atrophy, and fibrillation in one or both legs. In some males the sexual function was moderately impaired. Many patients developed trophic ulcers.

In those cases in which autopsy material was available, no definite macroscopic cord or caudal changes were found, but some of the cords showed increased hyalinization of the vessels and some marginal pallor. The Marchi stain revealed no definite change. Some of the sacral nerve roots showed a fine vacuolization, thought to be evidence of recent degeneration.

Direct trauma to the conus or nerves, hematoma formation, or inflammatory reaction were not held responsible for the complications; the alcohol and glycerine, likewise, were not thought to be the damaging agent. Rather, the toxic effect of the anesthetic itself was held to be the causative factor. The authors think that procaine in combination with alcohol and glycerine (and gliadin or gum acacia) injected in full strength in the caudal area exerts, in susceptible individuals, a toxic, degenerative effect on the rootlets where it is first deposited and held for a time in full concentration before it has become diluted by cerebrospinal fluid. They deprecate the use of heavy duracaine in its present form.

JOHN MARTIN, M.D.

PHYSICOCHEMICAL METHODS IN SURGERY

ROENTGENOLOGY

Bignami, C.: Roentgenological Technique and Anatomy of the Pyramid of the Temporal Bone (Tecnica ed anatomia radiografica della piramide temporale). *Radiol. med.*, 1938, 25: 495.

From an accurate study of the roentgenological visualization of the pyramid of the temporal bone, Bignami concludes that it is impossible to make a satisfactory projection by means of which this structure can be adequately visualized in all of its details and anatomical relationships. This is primarily due to the hidden position of this bony process within the cranial vault and also to the multiplicity of surrounding or superimposed structures presenting various degrees of density.

In order to enable the roentgenologist to obtain a satisfactory visualization of the osseous framework of the inner ear, it is necessary to obtain a series of pictures, each showing the various portions of this bone taken at a different angle. Control pictures of the healthy opposite side should also be obtained for comparison.

In selecting the various exposures, the author proposes the taking of a standard series based on fundamental criteria in order that unnecessary expense and labor be avoided. This series should enable the roentgenologist (a) to ascertain the position of the pyramid and to establish its anatomical relations to other structures; (b) to visualize the various faces and margins of the apex; (c) to visualize clearly the structures of the internal cavities and of the system of air cells; and (d) to compare the films with those of the opposite healthy side.

Fig. 2. X-ray film obtained by Schueller's technique; (1) mastoid cells, (2) antrum and periantral region, (3) region of labyrinth, (4) condyle of mandible, (5) external and internal acoustic meatus appearing almost concentrically one within the other.

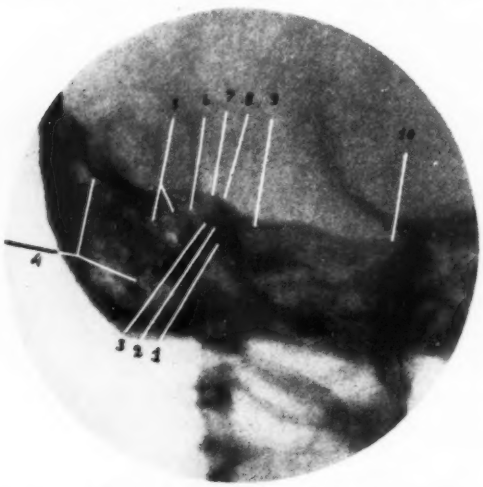

Fig. 1. X-ray film obtained by Stenvers' projection; (1) cochlea, (2) vestibule, (3) posterior semicircular canal, (4) mastoid cells, (5) borders of lateral sinus, (6) region of antrum and periantral cells, (7) tegmen labyrinthi, (8) superior semicircular canal, (9) internal acoustic meatus, and (10) apex of petrous bone.

The various standard projections proposed by the author for an adequate roentgenological series include:

(a) Stenvers' projection (occipitozygomatic plane)
(b) Schueller's projection (temporotympanic plane, also called transversal oblique plane)
(c) Axial submento-bregmatic plane
(d) Sagittal anteroposterior transorbital plane

Figures 1 and 2 show x-ray films taken according to Stenvers' and Schueller's technique, respectively.

The following exposures may be necessary also for a more complete visualization of the petrous portion of the temporal bone, of the mastoid region, and of the air-cell system:

(a) Fronto-suboccipital plane (Worms' and Breton's projection)
(b) Mayer's projection (Bregmatic-temporal plane)
(c) Ceresole's and Malcangi's projection (sagittal-oblique plane)

Figure 3 shows the x-ray film taken according to Mayer's technique.

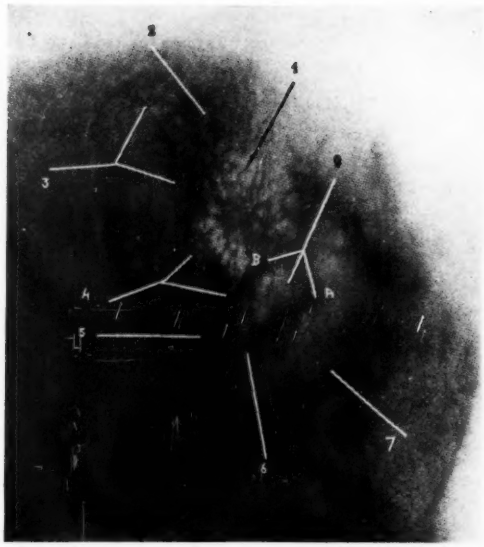

Fig. 3. X-ray film obtained by Mayer's technique; (1) periantral cells, (2) mastoid cells of the base, (3) anterior border of lateral sinus, (4) aditus ad antrum, (5) region of semicircular canals, (6) tympanic cavity, (7) condyle of mandible, (8) portion of the attic projected upon the medial extremity of the external acoustic meatus of which the anterior wall (A) and the posterior wall (B) can be clearly seen.

This standard series includes, in the author's opinion, all the exposures required to obtain a clear visualization of the pyramid, but in some cases additional films may be necessary.

The indications for the various techniques employed are the following:

1. Stenvers' projection complemented by Mayer's projection permits an accurate study of the form and the pathological processes of the petrous portion of the temporal bone, including its superior profile, the labyrinth, and the apex.

2. Schueller's and Ceresole-Malcangi's projections are best suited for the visualization of the mastoid process and the air-cell system.

3. Mayer's projection is especially useful for the visualization of pathological processes involving the periantral region.

4. Visualization of the lateral sinus and its relations to the system of air cells is best obtained by Schueller's, Stenvers', or Mayer's projections.

RICHARD E. SOMMA, M.D.

Solis-Cohen, L., and Levine, S.: X-Ray Diagnosis of Complete and Partial Acute Intestinal Obstruction. *Radiology*, 1938, 31: 8.

The authors believe that the radiologist can make a correct diagnosis in early cases of obstruction, which the clinician may not be able to do even after thorough examination. Ochsner proved that strangulated obstruction can be demonstrated with x-rays after one hour, and simple obstruction after three hours. He concluded that an accumulation of gas is the first sign rather than an accumulation of gas and fluid. In all suspected cases of ileus the authors routinely take three views, the anteroposterior, the postero-anterior, and the upright. They believe that the anteroposterior view is the most valuable for the differentiation of the large bowel from the small.

The first x-ray signs in an incipient case of ileus of mechanical origin are the presence of trapped gas and what is termed the "hairpin turn." The persistent appearance of a dilated loop of small bowel on successive films at hourly intervals is, in the opinion of the authors, evidence of an oncoming ileus. A dilated "hairpin turn" in the small bowel is the beginning of the so-called "step-ladder appearance," and in its presence a developing ileus must be suspected.

The significance of intestinal gas within both the small intestine and colon is as follows:

If the entire colon is dilated and only a small amount of air is seen in the small bowel, obstruction of the small intestine can be excluded. Tremendous dilatation of the colon, or a part of it, associated with

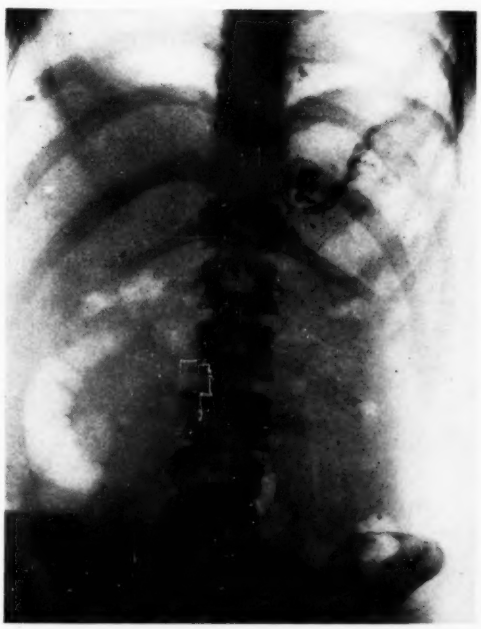

Fig. 1. Note the distended small intestinal loops in right lower quadrant due to intestinal obstruction produced by postoperative adhesions.

fluid levels and the absence of gas in the small intestine is indicative of obstruction of the large intestine. It is sometimes difficult to differentiate between the large and small bowel.

Morphine produces a general atonicity of the intestinal tract, and its effects may be manifested by large accumulations of gas, both in the colon and in the small bowel. The distribution of gas permits the differentiation of morphinization from ileus.

Fluid levels in the obstructed bowel are apparently late signs of obstruction and are due to intestinal hypersecretion. The higher the obstruction is situated, the greater the amount of fluid present. Marked distention of loops of the small bowel points to a high obstruction. The typical "step-ladder appearance" is a late sign of obstruction. The presence of striations in the mucosa indicates jejunal obstruction, while the ileum is relatively free of valvulæ conniventes. Duodenal or jejunal obstruction due to subhepatic collections is typified by marked distention of proximal loops of the small intestine and gastric dilatation.

The differentiation of adynamic ileus, peritonitis, and mechanical obstruction may be impossible by roentgenography alone. Dynamic ileus is diffuse and generalized and usually presents marked dilatation of the bowel. Carcinomatosis has been diagnosed roentgenologically by the observation of features of obstruction with a generalized haze throughout the abdomen, coupled with a fading or complete blotting out of the psoas shadows.

While the roentgenologist may venture an opinion as to whether the obstruction is high or low, most often he cannot state definitely in which quadrant of the abdomen the lesion is situated.

HAROLD C. OCHSNER. M.D.

MISCELLANEOUS

CLINICAL ENTITIES—GENERAL PHYSIOLOGICAL CONDITIONS

Telford, E. D., and Simmons, H. T.: Chronic Lymphedema. *Brit. J. Surg.*, 1938, 25: 765.

A classification of chronic lymphedema, based on history and clinical features, is suggested as follows: (1) Milroy's hereditary edema; (2) congenital edema; (3) obstructive edema; (4) post-traumatic edema; and (5) spontaneous edema.

Milroy's hereditary edema. This condition appears to be one of great rarity. Milroy's patient gave a genealogical history to the sixth generation; of 97 individuals, no less than 22 had suffered from chronic edema. The patient was a man thirty-one years of age, of good physique, who suffered from a chronic edema of both legs, to the level of the knees. The condition was stationary and had been present since birth. A study of Milroy's report suggests that the condition he described was probably a diffuse lymphatic hygroma of congenital origin. The familial transmission of such angiomatous mishaps is well known.

Congenital edema. The authors have seen a number of patients with this type of lymphedema in the feet and legs, and on the dorsum of the trunk. In 1 patient there was edema of the arm and leg on the same side.

This form of the condition appears to be a diffuse lymphatic hygroma analogous to the type occasionally seen in the neck of infants (cystic hygroma or hydrocele colli). It no doubt represents a congenital aberration in the development of lymphatic vessels analogous to that which results in the case of capillaries and venules, in venous nævi, and, like these, it may be localized or diffuse.

Obstructive edema. The cause of this type of edema is a capillary lymphangitis of widespread nature, due in many cases to streptococcal infection and followed by a diffuse perilymphatic fibrosis. The condition is seen after frank streptococcal infections, such as erysipelas, and is best known in relation to filarial infestations in man. It appears more likely that the resulting elephantiasis is due to the inflammatory reaction rather than to mechanical obstruction by the parasites themselves. In this group are also those edemas of the arms, secondary to massive involvement of the axilla by new growths. A similar condition is often seen as the result of post-radiation fibrosis.

Post-traumatic edema. In most of the recorded cases, the injury is a blunt trauma of no great severity and without open lesions of the tissues, but in some instances this condition has been reported following dog and cat bites.

Regarding the mechanism of the production of the edema, all that can be said at present is that for some unknown reason the normal process of repair following a contusion fails, and a disorder of the lymphatic mechanism is initiated at the site of injury, which may spread up and down the limb. Whether this disorder is an embarrassed return flow or an increased output is not clear, but the authors' cases have shown a considerable delay in the excretion of dyes following their local injection.

The clinical and operative appearances and findings are exactly the same as those described in spontaneous edema.

Spontaneous edema. It must be admitted that this type has no clear-cut diagnostic features. It differs from the other types in that no definite cause is apparent; the condition occurs in both sexes, and appears to arise at all ages. The edema develops insidiously as a puffiness about the ankle, spreads slowly upwards, and may eventually involve the skin of the abdomen and trunk. The limb may after some years reach an enormous size, but it remains of normal color and is not liable to the chronic ulceration which is found so frequently in the "white leg." The disease is more commonly unilateral, but in some instances the other leg is eventually involved. The skin is much thickened, the subcutaneous fatty tissue is enormously increased in depth, and the deep fascia is thickened. The disease never penetrates below the deep fascia.

The treatment of chronic lymphedema is discussed. Methods such as rest, massage, and elastic pressure give purely palliative and fugitive results. Surgery approaches the attack on lymphedema by one of two ways: (1) the attempt to utilize the normal lymph paths beneath the deep fascia (Kondoleon), and (2) the use of some form of sympathectomy.

Since 1930, the authors have performed the Kondoleon operation on 6 patients with chronic lymphedema in the lower limbs, and have been able to examine the results in 5 of these patients. In the case of only 1 patient was the result satisfactory. However, it is noteworthy that in 3 of the patients who were operated upon previously, six, five, and four years, respectively, further upward progress of the disease has been arrested.

Since August, 1936, 5 patients with chronic lymphedema of the lower extremity have been subjected to sympathectomy. The operation consisted of lumbar cord ganglionectomy involving the chain opposite the second, third, and fourth lumbar bodies. The end-results of this operation in lymphedema have been most disappointing. During the three weeks following the operation a remarkable shrinking of the limb occurred, much greater than is ever produced by rest alone; but once walking and work were resumed the limb quickly reverted to its pre-operative size and shape.

The authors conclude that lumbar cord ganglionectomy (and by inference any lesser form of

sympathectomy) has no place in the treatment of chronic lymphedema of the extremities.

JOHN H. GARLOCK, M.D.

Slome, D., and O'Shaughnessy, L.: The Nervous Factor in Traumatic Shock. *Brit. J. Surg.*, 1938, 25: 900.

The authors believe that their previous experiments eliminated toxemia as a causal factor of traumatic shock, and they were left with the problem of two remaining factors: fluid loss at the site of trauma, and the production of nervous impulses in that area. A series of 103 experiments is reported in which attention has been confined to the establishment of the rôle of the relative importance of fluid loss and the nervous factor. Cross circulation, blood transfusion, spinal anesthesia, and amputation experiments are the basis for the following conclusions:

The initial effect of trauma is either a pressor effect or a depressor effect. The latter effect is observed when there is definite marked muscle damage with consequent large fluid loss. The initial fall is absent (1) in the case of trauma with ligature of the arteries to the limb, and (2) in trauma to a limb that is kept alive by cross-circulation experiments, or by perfusion with the Dale-Schuster pump. The initial fall is present in experiments in which the nervous factor is controlled. It is present when trauma is applied after spinal anesthesia, or after cocainization or section of the nerves from the limbs traumatized. The initial fall in pressure, when present, must be attributed, therefore, to the loss of fluid from the circulation and to hemorrhage into traumatized tissues.

The subsequent gradual decline of the pressure cannot be attributed to the continued operation of the fluid loss, as it is absent (1) when trauma is applied under spinal anesthesia, (2) when trauma is applied to the denervated limb, and (3) when the perfused denervated limb is traumatized; and it is present when the nervous factor is operating, when no fluid loss can occur, as in the experiments in which trauma is applied to a limb kept alive by cross circulation or perfusion and connected to the animal only by neural connections. The initial depressor effect of trauma is due to fluid loss; the significant secondary decline to shock is caused by the continued and continuous discharge of nervous impulses from the traumatized area. The nervous factor operating alone can cause death. The fluid loss in these experiments, provided the nervous factor is controlled, is not fatal. The authors regard this concept of the late development and persistence of the nervous barrage as of fundamental importance in the understanding of the etiology of surgical shock.

HAROLD OCHSNER, M.D.

Lister, W. A.: The Natural History of Strawberry Nævi. *Lancet*, 1938, 234: 1429.

Strawberry nævi, commonly called cavernous angiomas, are always raised to some extent above the general level of the skin. They are present at birth or appear soon afterward. They grow more or less rapidly during the first few months of life, and thereafter invariably retrogress and disappear completely, at about the fifth year of life, leaving little or no trace.

Essentially, the lesion consists of an area of excessive vascularity. The redundant vessels may be situated in the superficial layers of the skin only, or may be confined to the deeper layers and subcutaneous tissue. Commonly, all sites are involved to a varying degree. The clinical appearance depends upon the site mainly affected. Even the most superficial type of nævus is always somewhat raised above the surrounding skin. The surface is finely lobulated, the color is commonly a vivid crimson, but ranges from a bright scarlet to a deep purple, and the nævus becomes more prominent and the color more intense when the child strains or cries. In consistency it is soft and boggy. When the deeper layers of the skin and the subcutaneous tissue are involved, it appears as a soft, rounded, or lobulated elevation, showing a faint purple or lilac tinge. When both superficial and deep sites are involved, it may be compared to a poached egg, the yolk being represented by the central crimson nodular zone of superficial vascularity which is superimposed upon a more extensive base of the deeper type, corresponding to the white of the egg.

Strawberry nævi of infants have a natural history all of their own, entirely different from that of any other type. The essential point of distinction is that they enjoy a period of more or less rapid growth during the first few months after their appearance. This never continues for more than a year, and usually ceases between the sixth and eighth months. Thereafter retrogression sets in. Usually, all traces of color have been obliterated by the fifth year, if not earlier, and only in the most prominent nævi is a further term of years required for the final absorption of redundant skin. This is the explanation of the uniformly good results recorded by operators, whatever may have been the method of treatment employed.

The physician's attitude toward the treatment of strawberry nævi must be based on the knowledge of their invariable tendency toward spontaneous retrogression. It is easy to be stampeded into advising drastic and injudicious measures. If the nævus is relatively small and in such a location that its destruction will not entail the risk of sepsis, or leave a scar which might be unsightly or disabling, it is as well to obliterate it forthwith. Radical destruction of a nævus is unjustifiable if the lesion is so placed that the resulting inevitable scar is in the least likely to cause disability or disfigurement. Still more are radical destructive measures contra-indicated when the nævus is found to be very large, for here such methods must, at the least, produce more or less gross disfigurement, and, at the worst, they may give rise to either fatal sepsis or hemorrhage.

Occasionally active treatment will be demanded, and then probably the wisest plan is to employ such measures as minimal exposure to radium, or the injection of small quantities of sclerosing fluid, the application of a firm dressing, or painting with collodion or Unna's paste. Whatever is done must be so slight as to be entirely free from any risk of causing a scar. This line of treatment is made all the easier because the appearance of the nævus at any particular age can be more or less accurately foretold, and the parents' confidence can be gained.

If a nævus shows no active growth in infancy, it is unlikely to retrogress of its own accord. It may not start to grow for many years, and then only very slowly. It can be dealt with deliberately when the child is older. SAMUEL KAHN, M.D.

Davis, L., and Barker, M. H.: The Surgical Problem of Hypertension. *Ann. Surg.*, 1938, 107: 899.

This paper is a preliminary report, the purpose of which is to set forth the approach which these investigators use in their attack on the problem of the surgical treatment of hypertension. They state that hypertension has been produced experimentally in four ways: (1) by removal of the carotid sinus and the cardio-aortic moderator nerves (Heymans); (2) by the production of renal ischemia (Goldblatt); (3) by the production of cerebral anemia and anoxemia of the vasopressor centers; and (4) by the administration of Vitamin D. They have not been able to correlate the hypertension of human subjects with the anatomical and physiological changes noted in animals in which hypertension has been produced by any of these methods—a matter which has been of concern to many American clinicians since the advent of Goldblatt's method of producing hypertension. They point out that an adequate definition of hypertension has not yet been found, and that even a clear distinction between essential and malignant hypertension has not yet been attained.

An urgent need is felt for reliable criteria on which patients with hypertension may be selected for surgical treatment. In their own series of cases they have chosen only relatively young hypertensive patients without renal damage, whose blood pressures under normal conditions show rather marked fluctuations, whose vascular tree is still elastic, and who, after adequate trial, have been found to be insensitive to cyanate therapy. After a long period of observation as out-patients, they are admitted to the hospital for more critical study. Renal function tests, detailed blood-chemistry studies, detailed charts of blood pressures under all conditions found in the twenty-four-hour schedule of the patient, the "cold pressor" test, and vasodilator tests with the use of drugs are all accomplished. In addition, blood-pressure readings are made during the administration of carbon dioxide. Not until all these data are complete and analyzed is the patient considered from the standpoint of surgical therapy. Early results obtained by the authors suggest that cyanate-resistant patients become more cyanate-sensitive following splanchnic resection.

Davis and Barker believe that neither the rationale nor the results of many operations performed in the past for hypertension are susceptible to an accurate physiological explanation, and that many of the results are not conclusive. They believe that clinical investigations must be conducted on anatomical and physiological principles, in the same manner that any laboratory experiment would be carried out. JOHN MARTIN, M.D.

Gurney, C. E.: Experimental Study of the Behavior of Free Fat Transplants. *Surgery*, 1938, 3: 679.

There are certain clinical problems associated with the transplantation of fat which justify further experimental study. It is well known that practically all fat grafts gradually diminish in size following their transplantation.

Experimental studies designed to show the behavior of free transplants of fat were made on 185 white adult rats of average size. In each instance subcutaneous or peritoneal fat was transferred to a subcutaneous pocket in the thoracic region. The rats were divided into five groups, depending on the treatment received by the graft immediately prior to its transplantation. Group A comprised the rats in which autotransplants of fat of the groin were transferred as a single piece without trauma. Group B included those in which autotransplants of fat of the groin were cut into multiple pieces with a sharp razor. Group C included those in which autotransplants of fat of the groin were severely traumatized by squeezing with a hemostat. Group D comprised those in which homotransplants of fat of the groin were transferred without trauma. Group E included those in which autotransplants of fat obtained from the peritoneal cavity were transferred without trauma.

The rats in the first four groups were killed at intervals of one, two, and three weeks, and one, two, three, four, six, nine, and twelve months after the operation. In the last group they were killed one week, and one, four, nine, and twelve months after the operation. At each examination the surviving grafts were studied grossly and microscopically. All of the sections were stained with sudan III and a few were stained with hematoxylin and eosin.

The outstanding gross finding was that almost without exception those autografts which were transplanted as a single piece without trauma (Groups A and E) retained their identity throughout the whole year of observation. Those autografts which were cut into multiple pieces or crushed (Groups B and C) survived for a shorter period. Except for two grafts the transplants in both groups had completely disappeared after four months. The homografts (Group D) survived only for a very short time. Not the slightest suggestion of a graft was found after three months.

All of the grafts were soft to palpation for the first day or two after operation. About the third or

fourth day they began to enlarge, and became more firm and globular. By the second week they began to recede, and by one month they were soft and much smaller than they were when transplanted. Gross infection occurred in 7 cases and in all except 1 the infection occurred in those grafts which had been subjected to cutting or crushing. The cut surface of most of the grafts presented a gray homogenous appearance not unlike that of normal fat. The grafts composed of multiple pieces and those which had been subjected to crushing were much more oily. Minute droplets of fat exuded from the cut surface of these grafts. There was no complete liquefaction of the graft as occasionally is seen clinically.

The microscopic findings were characterized by degenerative changes in all of the grafts. The most violent and extensive reaction was seen in the homotransplants (Group D). Those grafts composed of multiple pieces and those which had been crushed (Groups B and C) were subjected to a less violent reaction, while those grafts which had been carefully transplanted as a single piece, without trauma, showed the least degenerative change.

The degenerative changes were manifested by a disappearance of the nucleus of the fat cell; a disintegration of the wall of the cell; the formation of cysts and vacuoles; infiltration of polymorphonuclear leucocytes, lymphocytes, and histiocytes; phagocytosis; and a gradual reduction in the size of the graft, which in some instances continued until the graft disappeared entirely.

The fat cells in certain portions of the graft appeared normal except for the absence of their nuclei. This finding was most noticeable in the homografts one week after operation; this change involved most of these grafts. In the other groups it occurred only in portions of the grafts, especially about the periphery.

A definite, but futile, search was made to find new fat cells which would lend support to the assertion that regeneration of fat is the rule after transplantation. All of the fat appearing in the grafts as viable tissue was composed of normal adult fat cells. New blood vessels were visible as early as one week in the autografts which had been made without trauma. They could be followed at succeeding examinations and at nine and twelve months the grafts were well vascularized. No new vessels were observed in any of the homografts and rarely in the autografts which had been subjected to trauma. During the first month, only a small percentage of the implant contained normal fat, but in one year about 90 per cent of the graft appeared to be normal.

These experiments do not justify the opinion that multiple small pieces of fat survive better than does a single large piece. They show that single pieces remain viable for at least one year, while original grafts of a similar size and composed of several smaller pieces of fat, may last as long as six months, but the majority disappear by the third month. The transplants which were obtained from the groin averaged 23 per cent of their original size and those which were obtained from the abdominal cavity, 51 per cent of their original size.

Among the conclusions were the following statements:

Subcutaneous fat is a suitable tissue for autotransplantation if proper precautions are taken at the time of transplantation. Although peritoneal fat survives better than subcutaneous fat, the accessibility and successful use of the latter give it preference in the average case. A much larger piece of fat must be transplanted than would at first seem necessary, since only from one-fourth to one-half of the graft survives. The fat comprising the graft at one year after operation is a portion of the original transplanted fat. If that portion of the fat which disappears becomes scar tissue, this also ultimately disappears, since the site of the transplant is not marked grossly by scar tissue.